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Trying 31060000009999...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
 ******** HHHHHHHH SSSSSSSS? ### Status: Signing onto Dialog ********
ENTER PASSWORD:
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### Status: Login successfulDialog level 05.15.00D

Last logoff:  05jan07 15:02:16
Logon file405 23jan07 12:45:47
           *** ANNOUNCEMENTS ***
                    ***
NEW FILES RELEASED
***Engineering Index Backfile (File 988)
***Verdict Market Research (File 769)
***EMCare (File 45)
***Trademarkscan - South Korea (File 655)

RESUMED UPDATING
***File 141, Reader's Guide Abstracts
                   ***
RELOADS COMPLETED
***Files 340, 341 & 942, CLAIMS/U.S. Patents - 2006 reload now online
***Files 173 & 973, Adis Clinical Trials Insight
***File 11, PsycInfo
***File 531, American Business Directory
                                ***
DATABASES REMOVED
***File 196, FINDEX
***File 468, Public Opinion Online (POLL)
Chemical Structure Searching now available in Prous Science Drug
Data Report (F452), Prous Science Drugs of the Future (F453),
IMS R&D Focus (F445/955), Pharmaprojects (F128/928), Beilstein
Facts (F390), Derwent Chemistry Resource (F355) and Index Chemicus
(File 302).
                   ***
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* * *
SYSTEM:HOME
Cost is in DialUnits
Menu System II: D2 version 1.8.0 term=ASCII
                     *** DIALOG HOMEBASE(SM) Main Menu ***

 Information:
  1.  Announcements (new files, reloads, etc.)
  2.  Database, Rates, & Command Descriptions
  3.  Help in Choosing Databases for Your Topic
  4.  Customer Services (telephone assistance, training, seminars, etc.)
  5.  Product Descriptions

 Connections:
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  6.  DIALOG(R) Document Delivery
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      /H = Help            /L = Logoff          /NOMENU = Command Mode

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 service.  Enter a BEGIN command plus a file number to search a database
(e.g., B1 for ERIC).
?
Terminal set to DLINK
                    *** DIALOG HOMEBASE(SM) Main Menu ***

 Information:
  1.  Announcements (new files, reloads, etc.)
  2.  Database, Rates, & Command Descriptions
  3.  Help in Choosing Databases for Your Topic
  4.  Customer Services (telephone assistance, training, seminars, etc.)
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      /H = Help            /L = Logoff          /NOMENU = Command Mode

Enter an option number to view information or to connect to an online
 service.  Enter a BEGIN command plus a file number to search a database
(e.g., B1 for ERIC).
? b biosci

>>>          44 is unauthorized
>>>          76 is unauthorized
>>>2 of the specified files are not available
       23jan07 12:45:52 User276653 Session D80.1
            $0.00    0.245 DialUnits FileHomeBase
     $0.00  Estimated cost FileHomeBase
     $0.02  TELNET
     $0.02  Estimated cost this search
     $0.02  Estimated total session cost   0.245 DialUnits


SYSTEM:OS  - DIALOG OneSearch
  File   5:Biosis Previews(R) 1969-2007/Jan W2
         (c) 2007 The Thomson Corporation
  File  24:CSA Life Sciences Abstracts 1966-2007/Nov
         (c) 2007 CSA.
  File  28:Oceanic Abstracts 1966-2007/Nov
         (c) 2007 CSA.
  File  34:SciSearch(R) Cited Ref Sci 1990-2007/Jan W2
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  File  35:Dissertation Abs Online 1861-2006/Nov
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File 45:EMCare 2007/Jan W2
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(c) 2007 CAB International
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File 71:ELSEVIER BIOBASE 1994-2007/Jan W3
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File 73:EMBASE 1974-2007/Jan 17
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***File 73: Elsevier will not provide the daily update to Embase on January 18. Tomorrow's update will contain both days.**
File 91:MANTIS(TM) 1880-2006/Jan
2001 (c) Action Potential
File 94:JICST-EPlus 1985-2007/Jan W3
(c)2007 Japan Science and Tech Corp(JST)
***File 94: UD200609W2 is the last update for 2006. UD200701W1 is the first update for 2007. The file is complete and up to date.**
File 98:General Sci Abs 1984-2007/Jan
(c) 2007 The HW Wilson Co.
File 110:WasteInfo 1974-2002/Jul
(c) 2002 AEA Techn Env.
***File 110: This file is closed (no updates)**
File 135:NewsRx Weekly Reports 1995-2007/Jan W2
(c) 2007 NewsRx
File 136:BioEngineering Abstracts 1966-2007/Nov
(c) 2007 CSA.
File 143:Biol. & Agric. Index 1983-2007/Dec
(c) 2007 The HW Wilson Co
File 144:Pascal 1973-2007/Jan W2
(c) 2007 INIST/CNRS
File 155:MEDLINE(R) 1950-2006/Dec 16
(c) format only 2006 Dialog
***File 155: MEDLINE has resumed updating with UD20061209. Please see HELP NEWS 154 for details.**
File 164:Allied & Complementary Medicine 1984-2007/Jan
(c) 2007 BLHCIS
File 172:EMBASE Alert 2007/Jan 23
(c) 2007 Elsevier B.V.
File 185:Zoological Record Online(R) 1978-2007/Feb
(c) 2007 The Thomson Corp.
File 357:Derwent Biotech Res. _1982-2007/Jan W1
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File 369:New Scientist 1994-2007/Oct W3
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File 370:Science 1996-1999/Jul W3
(c) 1999 AAAS
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File 391:Beilstein Reactions 2006/Q4
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File 467:ExtraMED(tm) 2000/Dec
(c) 2001 Informania Ltd.

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      Set   Items   Description
      ---   -----   -----------
? s crystallin
      S1    40380   CRYSTALLIN
? s arginine(n)chloride
           416125   ARGININE
          1978652   CHLORIDE
      S2      483   ARGININE(N)CHLORIDE
? s s1 and s2
            40380   S1
              483   S2
      S3        1   S1 AND S2
? t s3/9,k/all
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3/9,K/1 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

13167229 EMBASE No: 2005234088

Alexander-disease mutation of GFAP causes filament disorganization and decreased solubility of GFAP

Hsiao V.C.; Tian R.; Long H.; Perng M.D.; Brenner M.; Quinlan R.A.; Goldman J.E.

J.E. Goldman, Department of Pathology, Center for Neurobiology and Behavior, Columbia University, New York, NY 10032 United States
AUTHOR EMAIL: jeg5@columbia.edu

Journal of Cell Science (J. CELL SCI.) (United Kingdom) 01 MAY 2005, 118/9 (2057-2065)
CODEN: JNCSA ISSN: 0021-9533
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 66

Alexander disease is a fatal neurological illness characterized by white-matter degeneration and the formation of astrocytic cytoplasmic inclusions called Rosenthal fibers, which contain the intermediate filament glial fibrillary acidic protein (GFAP), the small heat-shock proteins HSP27 and alphaB- **crystallin** , and ubiquitin. Many Alexander-disease patients are heterozygous for one of a set of point mutations in the GFAP gene, all of which result in amino acid substitutions. The biological effects of the most common alteration, R239C, were tested by expressing the mutated protein in cultured cells by transient transfection. In primary rat astrocytes and Cos-7 cells, the mutant GFAP was incorporated into filament networks along with the endogenous GFAP and vimentin, respectively. In SW13VimSUP- cells, which have no endogenous cytoplasmic intermediate filaments, wild-type human GFAP frequently formed filamentous bundles, whereas the R239C GFAP formed 'diffuse' and irregular patterns. Filamentous bundles of R239C GFAP were sometimes formed in SW13VimSUP- cells when wild-type GFAP was co-transfected. Although the presence of a suitable coassembly partner (vimentin or GFAP) reduced the potential negative effects of the R239C mutation on GFAP network formation, the mutation affected the stability of GFAP in cells in a dominant fashion. Extraction of transfected SW13VimSUP- cells with Triton-X-100-containing buffers

showed that the mutant GFAP was more resistant to solubilization at elevated KCl concentrations. Both wild-type and R239C GFAP assembled into 10 nm filaments with similar morphology in vitro. Thus, although the R239C mutation does not appear to affect filament formation per se, the mutation alters the normal solubility and organization of GFAP networks.

DRUG DESCRIPTORS:
*glial fibrillary acidic protein--endogenous compound--ec
heat shock protein 27--endogenous compound--ec; alpha **crystallin** --endogenous compound--ec; beta **crystallin** --endogenous compound--ec; ubiquitin--endogenous compound--ec; amino acid--endogenous compound--ec; mutant protein--endogenous compound--ec; vimentin--endogenous compound--ec; triton x 100; buffer; potassium **chloride** ; **arginine** --endogenous compound --ec; cysteine--endogenous compound--ec
MEDICAL DESCRIPTORS:
*Alexander disease--diagnosis--di; *Alexander disease--etiology--et gene mutation; neurologic disease--etiology--et; clinical feature; white matter; astrocyte; cell inclusion; heterozygosity; point mutation; amino acid substitution; protein expression; cell culture; genetic transfection; cytoplasm; wild type; protein assembly; intermediate filament; protein stability; solubilization; concentration (parameters); cell structure; in vitro study; protein structure; human; nonhuman; rat; controlled study; human cell; animal cell; article; priority journal
CAS REGISTRY NO.: 60267-61-0 (ubiquitin); 65072-01-7 (amino acid); 7447-40-7 (potassium chloride); 1119-34-2, 15595-35-4, 7004-12-8, 74-79-3 (arginine); 4371-52-2, 52-89-1, 52-90-4 (cysteine)
SECTION HEADINGS:
  005 General Pathology and Pathological Anatomy
  008 Neurology and Neurosurgery
  022 Human Genetics
  029 Clinical and Experimental Biochemistry

...intermediate filament glial fibrillary acidic protein (GFAP), the small heat-shock proteins HSP27 and alphaB- **crystallin** , and ubiquitin. Many Alexander-disease patients are heterozygous for one of a set of point
...
DRUG DESCRIPTORS:
heat shock protein 27--endogenous compound--ec; alpha **crystallin** --endogenous compound--ec; beta **crystallin** --endogenous compound--ec; ubiquitin--endogenous compound--ec; amino acid--endogenous compound--ec; mutant protein--endogenous compound--ec; vimentin--endogenous compound--ec; triton x 100; buffer; potassium **chloride** ; **arginine** --endogenous compound --ec; cysteine--endogenous compound--ec
? s arginine and chloride
          416125 ARGININE
         1978652 CHLORIDE
      S4   12788 ARGININE AND CHLORIDE
? s s1 and s4
           40380 S1
           12788 S4
      S5   10 S1 AND S4
? t s5/9,k/1-10

 5/9,K/1   (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05956303 Genuine Article#: XK290 Number of References: 42
Title: Expression of arginine decarboxylase in seedlings of indica rice (Oryza sativa L) cultivars as affected by salinity stress
Author(s): Chattopadhyay MK; Gupta S; Sengupta DN; Ghosh B (REPRINT)
Corporate Source: BOSE INST,DEPT BOT, 93-1 APC RD/CALCUTTA 700009/W BENGAL/INDIA/ (REPRINT); BOSE INST,DEPT BOT/CALCUTTA 700009/W BENGAL/INDIA/
Journal: PLANT MOLECULAR BIOLOGY, 1997, V34, N3 (JUN), P477-483
ISSN: 0167-4412 Publication date: 19970600
Publisher: KLUWER ACADEMIC PUBL, SPUIBOULEVARD 50, PO BOX 17, 3300 AA DORDRECHT, NETHERLANDS
Language: English Document Type: ARTICLE
Geographic Location: INDIA
Subfile: CC LIFE--Current Contents, Life Sciences; CC AGRI--Current Contents, Agriculture, Biology & Environmental Sciences
Journal Subject Category: PLANT SCIENCES; BIOCHEMISTRY & MOLECULAR BIOLOGY
Abstract: The effect of salinity stress on the activity of **arginine** decarboxylase (ADC, EC 4.1.1.19), the first enzyme in biosynthesis of polyamines (PA) from **arginine** , as well as its transcript level has been compared in salt-sensitive (M-1-48) and salt-tolerant (Pokkali) rice cultivars. Treatment of 72 h grown seedlings either with increasing concentrations of NaCl or with 150 mM NaCl for different time periods, showed a gradual increase of activity in Pokkali. In M-1-48 an immediate increase followed by sharp decrease was observed on prolonged treatment beyond 6 h or above 150 mM NaCl. To generate a DNA probe for ADC, the polymerase chain reaction was used with oat genomic DNA and sequence-specific primers. A region of oat genomic DNA containing a coding sequence for 166 amino acids of the C-terminal part of the ADC enzyme was amplified and called OAD1. Southern analysis of EcoRI- or BamHI-cut genomic DNAs from different cultivars of rice with OAD1 as the probe revealed strong hybridization with one DNA fragment of rice and restriction fragment length polymorphism (RFLP) was noticed. Northern analysis of total RNA of rice with OAD1 as the probe revealed hybridization with a transcript of similar size to the ADC transcript in oat. While in Pokkali, at least a 20-fold accumulation of OAD1 homologous transcript was detected after treatment with 200 mM NaCl, only a seven-fold increase in transcript level was found in M-1-48 after 150 mM NaCl treatment. Results suggest that in the salt-tolerant rice cultivar Pokkali ADC enzyme activity increases and its transcript also accumulates during the prolonged salinity stress, this mechanism is absent in the salt-sensitive rice cultivar M-1-48 where a prolonged period of salinity stress down-regulates both ADC activity and its transcript level.
Descriptors--Author Keywords: **arginine** decarboxylase ; gene expression ; Oryza sativa ; polyamines ; rice ; salinity stress
Identifiers--KeyWord Plus(R): POLYAMINE ACCUMULATION; OSMOTIC-STRESS; SALT TOLERANCE; WATER-STRESS; LEAVES; PUTRESCINE; RESPONSES; PLANTS; ACID; **CHLORIDE**
Research Fronts: 95-1488 001 (ORNITHINE DECARBOXYLASE; SPERMIDINE TRANSPORT IN HUMAN BREAST-CANCER CELLS; REGULATION OF CELLULAR POLYAMINES)
95-3190 001 (INCREASED ABUNDANCE OF SPECIFIC SKELETAL-MUSCLE PROTEIN-TYROSINE PHOSPHATASES; ALPHA-B- **CRYSTALLIN** EXPRESSION)
95-3260 001 (ABSCISIC-ACID RESPONSE ELEMENTS; STRESS PROTEINS; GENE IN ARABIDOPSIS-THALIANA; DIFFERENTIAL EXPRESSION; POTENTIAL REGULATION; DESICCATION TOLERANCE)
95-5061 001 (STRUCTURAL GENE; GLTC-DEPENDENT REGULATION OF

BACILLUS-SUBTILIS GLUTAMATE SYNTHASE EXPRESSION; ARABIDOPSIS TYPE-1 PROTEIN PHOSPHATASE)
95-5565 001 (POLYAMINE BIOSYNTHESIS; DEVELOPMENT OF ZYGOTIC EMBRYOS; MOUSE ORNITHINE DECARBOXYLASE CDNA IN CARROT PROMOTES SOMATIC EMBRYOGENESIS)

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Title: Expression of arginine **decarboxylase in seedlings of indica rice (Oryza sativa L) cultivars as affected by salinity** stress

Abstract: The effect of salinity stress on the activity of **arginine** decarboxylase (ADC, EC 4.1.1.19), the first enzyme in biosynthesis of polyamines (PA) from **arginine** , as well as its transcript level has been compared in salt-sensitive (M-1-48...

...Identifiers--POLYAMINE ACCUMULATION; OSMOTIC-STRESS; SALT TOLERANCE; WATER-STRESS; LEAVES; PUTRESCINE; RESPONSES; PLANTS; ACID; **CHLORIDE**

...Research Fronts: POLYAMINES)
95-3190 001 (INCREASED ABUNDANCE OF SPECIFIC SKELETAL-MUSCLE

PROTEIN-TYROSINE PHOSPHATASES; ALPHA-B- **CRYSTALLIN** EXPRESSION)
95-3260 001 (ABSCISIC-ACID RESPONSE ELEMENTS; STRESS PROTEINS; GENE IN ARABIDOPSIS-THALIANA; DIFFERENTIAL...

5/9,K/2 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05799266 Genuine Article#: WY280 Number of References: 40
Title: Chronic ethanol increases N-methyl-D-aspartate-stimulated nitric oxide formation but not receptor density in cultured cortical neurons
Author(s): Chandler LJ (REPRINT) ; Sutton G; Norwood D; Sumners C; Crews FT
Corporate Source: LOUISIANA STATE UNIV,MED CTR, DEPT PHARMACOL, 1501 KINGS HIGHWAY/SHREVEPORT//LA/71130 (REPRINT); UNIV FLORIDA,COLL MED, DEPT PHYSIOL/GAINESVILLE//FL/32610; UNIV N CAROLINA,BOWLES CTR ALCOHOL STUDIES/CHAPEL HILL//NC/27599
Journal: MOLECULAR PHARMACOLOGY, 1997, V51, N5 (MAY), P733-740
ISSN: 0026-895X Publication date: 19970500
Publisher: WILLIAMS & WILKINS, 351 WEST CAMDEN ST, BALTIMORE, MD 21201-2436
Language: English Document Type: ARTICLE
Geographic Location: USA
Subfile: CC LIFE--Current Contents, Life Sciences
Journal Subject Category: PHARMACOLOGY & PHARMACY; BIOCHEMISTRY & MOLECULAR BIOLOGY
Abstract: The effects of prolonged ethanol exposure on excitatory amino acid receptor stimulated nitric oxide (NO) formation were examined in primary rat cortical neuronal cultures. Chronic ethanol (4 days, 100 mM) potentiated N-methyl-D-aspartate (NMDA)-stimulated NO formation as determined by measuring the conversion of [H-3] **arginine** to [H-3]citrulline. In contrast, chronic ethanol had no effect on NO formation stimulated by kainate, alpha-amino-3-hydroxy-5-methyl-4-isoxalonepropionic acid, or the calcium ionophore ionomycin. Potassium **chloride** -stimulated NO formation was also enhanced by chronic ethanol treatment, but this effect was not seen in the presence of the ionotropic glutamate receptor antagonists MK-801 and 6-cyano-7-nitroquinoxaline-2,3-dione. Immunoblot analysis of expression of NR1, NR2A, and NR2B receptor subunits showed no difference between control and chronic ethanol-treated cultures. In support of this apparent lack of change in receptor density, there was no difference in the specific binding of I-125-MK-801 between control and chronic ethanol-treated groups. These results demonstrate that prolonged ethanol exposure selectively enhanced NMDA receptor-stimulated NO formation, which may play an important role in alcohol dependence, withdrawal, and alcohol-associated brain damage. These results also suggest that chronic ethanol-induced increases in NMDA receptor function may not be due to a simple increase in the number of NMDA receptors or change in NMDA receptor subunit composition but may instead reflect more complicated and subtle changes.
Identifiers--KeyWord Plus(R): WITHDRAWAL SEIZURES; RAT-BRAIN; ALCOHOL-WITHDRAWAL; IONOPHORE COMPLEX; CHRONIC EXPOSURE; RAPID TOLERANCE; NMDA RECEPTORS; SYNTHASE; BINDING; SUBUNIT
Research Fronts: 95-3190 001 (INCREASED ABUNDANCE OF SPECIFIC

SKELETAL-MUSCLE PROTEIN-TYROSINE PHOSPHATASES; ALPHA-B- **CRYSTALLIN** EXPRESSION)
95-6313 001 (ETHANOL WITHDRAWAL; N-METHYL-D-ASPARTATE RECEPTORS; RAT HIPPOCAMPAL 2-DEOXYGLUCOSE UPTAKE IN-VITRO)

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...Abstract: D-aspartate (NMDA)-stimulated NO formation as determined by measuring the conversion of [H-3] **arginine** to [H-3]citrulline. In contrast, chronic ethanol had no effect on NO formation stimulated...

...alpha-amino-3-hydroxy-5-methyl-4-isoxalonepropionic acid, or the calcium ionophore ionomycin. Potassium **chloride** -stimulated NO formation was also enhanced by chronic ethanol treatment, but this effect was not...

Research Fronts: 95-3190 001 (INCREASED ABUNDANCE OF SPECIFIC SKELETAL-MUSCLE PROTEIN-TYROSINE PHOSPHATASES; ALPHA-B- **CRYSTALLIN** EXPRESSION)
95-6313 001 (ETHANOL WITHDRAWAL; N-METHYL-D-ASPARTATE RECEPTORS; RAT

5/9,K/3 (Item 3 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05765539 Genuine Article#: WW460 Number of References: 37

Title: Simulatory effect of porcine insulin on noradrenaline secretion in guinea-pig ileum myenteric nerve terminals

Author(s): Cheng JT (REPRINT) ; Hung CR; Lin MI
Corporate Source: NATL CHENG KUNG UNIV,COLL MED, DEPT PHARMACOL/TAINAN 70101//TAIWAN/ (REPRINT)

Journal: BRITISH JOURNAL OF PHARMACOLOGY, 1997, V121, N1 (MAY), P15-20
ISSN: 0007-1188 Publication date: 19970500
Publisher: STOCKTON PRESS, HOUNDMILLS, BASINGSTOKE, HAMPSHIRE, ENGLAND RG21 6XS
Language: English Document Type: ARTICLE
Geographic Location: TAIWAN
Subfile: CC LIFE--Current Contents, Life Sciences
Journal Subject Category: PHARMACOLOGY & PHARMACY; BIOCHEMISTRY & MOLECULAR BIOLOGY

Abstract: 1 The effect of insulin on the release of noradrenaline (NA) from nerve terminals was investigated in isolated ileal synaptosomes of guinea-pig. Release was determined as the amount of NA, quantified by h.p.l.c.-electrochemical detection, from samples incubated with insulin minus that in parallel blanks treated with some volume of vehicle.

2 Porcine insulin stimulated the secretion of NA in a concentration-dependent manner from 0.01 i.u. ml(-1), while the value of lactate dehydrogenase in the incubated medium was not influenced by insulin.

3 The presence of insulin receptors in this preparation was illustrated by immunoblotting with insulin receptor monoclonal antibodies.

4 The release of NA by insulin was reduced by guanethidine and bretylium and it was markedly lowered in the samples obtained from guinea-pigs that had received an intraperitoneal injection of DSP-4, the noradrenergic neurotoxin.

5 Tetrodotoxin attenuated the action of insulin at concentrations sufficient to block sodium channels. The depolarizing effect of insulin on the membrane potential was also illustrated by a concentration-dependent increase in the fluorescence of bisoxonol, a potential-sensitive dye.

6 The action of insulin was attenuated by removal of calcium **chloride** from the bathing medium. The induction of calcium ion influx by insulin into the synaptosomes is supported by the inhibitory effects of the calcium channel blockers omega-conotoxin GVIA (for the N-type channels) and nifedipine (for the L-type channels).

7 These findings suggest that insulin can stimulate NA release from noradrenergic terminals via activation of calcium influx.

Descriptors--Author Keywords: insulin ; noradrenaline release ; bisoxonol ; calcium influx ; synaptosomal preparation of guinea-pig ileum

Identifiers--KeyWord Plus(R): CYTOSOLIC CA-2+; HYPERTENSION; RATS; HYPERINSULINEMIA; CATECHOLAMINES; SYNAPTOSOMES; TETRODOTOXIN; ACTIVATION; INHIBITION; MEMBRANES
Research Fronts: 95-0917 002 (INSULIN-RESISTANCE IN SYSTEMIC HYPERTENSION; COMPENSATORY HYPERINSULINEMIA; CARDIOVASCULAR RISK; ELDERLY MEN)
95-3190 002 (INCREASED ABUNDANCE OF SPECIFIC SKELETAL-MUSCLE PROTEIN-TYROSINE PHOSPHATASES; ALPHA-B- **CRYSTALLIN** EXPRESSION)
95-0651 001 (CALCIUM CHANNELS; RAT CEREBELLAR GRANULE NEURONS; CA2+ RELEASE)
95-3958 001 (RAT ISOLATED ANOCOCCYGEUS MUSCLE; SCORPION TOXINS; VOLTAGE-GATED ION CHANNELS; L- **ARGININE** -NITRIC OXIDE PATHWAY INVOLVEMENT; RELAXANT RESPONSES)
95-5343 001 (CAMP-DEPENDENT PROTEIN-KINASE; SIGNALING SPECIFICITY; PHOSPHATE PROTECTION)
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...Abstract: a potential-sensitive dye.

6 The action of insulin was attenuated by removal of calcium

chloride from the bathing medium. The induction of calcium ion influx by insulin into the synaptosomes...
...Research Fronts: MEN)
95-3190 002 (INCREASED ABUNDANCE OF SPECIFIC SKELETAL-MUSCLE PROTEIN-TYROSINE PHOSPHATASES; ALPHA-B- **CRYSTALLIN** EXPRESSION)
95-0651 001 (CALCIUM CHANNELS; RAT CEREBELLAR GRANULE NEURONS; CA2+ RELEASE)
95-3958 001 (RAT ISOLATED ANOCOCCYGEUS MUSCLE; SCORPION TOXINS; VOLTAGE-GATED ION CHANNELS; L- **ARGININE** -NITRIC OXIDE PATHWAY INVOLVEMENT; RELAXANT RESPONSES)
95-5343 001 (CAMP-DEPENDENT PROTEIN-KINASE; SIGNALING SPECIFICITY...

5/9,K/4 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05675361 Genuine Article#: WP266 Number of References: 62
Title: The effect of hypotonicity, glutamine, and glycine on red cell preservation
Author(s): Greenwalt TJ (REPRINT) ; Rugg N; Dumaswala UJ
Corporate Source: UNIV CINCINNATI,MED CTR, HOXWORTH BLOOD CTR, DEPT RES, 3131 HIGHLAND AVE, POB 670055/CINCINNATI//OH/45267 (REPRINT)
Journal: TRANSFUSION, 1997, V37, N3 (MAR), P269-276
ISSN: 0041-1132 Publication date: 19970300
Publisher: AMER ASSOC BLOOD BANKS, 8101 GLENBROOK RD, BETHESDA, MD 20814-2749
Language: English Document Type: ARTICLE
Geographic Location: USA
Subfile: CC LIFE--Current Contents, Life Sciences; CC CLIN--Current Contents, Clinical Medicine
Journal Subject Category: HEMATOLOGY
Abstract: BACKGROUND: Red cells (RBCs) stored in hypo-osmolar additive solutions with the same concentrations of adenine, dextrose, mannitol, and sodium **chloride** and varied amounts of ammonium, phosphate, glycerol, and glutamine were better preserved than RBCs in the standard additive solution (Adsol). Cell swelling occurred in all the experimental additives. This observation prompted the evaluation of glutamine and glycine alone, as well as a combination of glutamine and glycine, all of which have been described as producing swelling of rat liver cells.

STUDY DESIGN AND METHODS: Aliquots of RBCs were stored at 4 degrees C in Adsol or experimental additive solutions (EASs) all containing adenine, 2 mM; dextrose, 110 mM; mannitol, 55 mM; and sodium **chloride** , 50 mM. EAS 42 had, in addition, glutamine, 10 mM; glycine 5 mM; and phosphate, 20 mM. EAS 43 had glutamine, 10 mM glycine, 10 mM; and phosphate 20 mM. EAS 44 had glutamine, 10 mM; EAS 45 had glutamine, 10 mM, and phosphate, 20 mM; and EAS 46 had only glycine, 10 mM. At intervals, measurements were made of mean corpuscular volume, mean corpuscular hemoglobin concentration, morphology, ATP, hemolysis, supernatant potassium, ammonia, pH, and microvesicles shed.

RESULTS: The initial mean corpuscular volumes were larger in all EASs than in Adsol, but the greatest difference was between EASs 44 and 46 (108 fL) and Adsol (86 fL) ($p<0.001$). The morphology scores were significantly better in all the EASs ($p<0.04$). The ATPs were

significantly greater in all the EASs ($p<0.001$), and highest in those with phosphate. Potassium leakage and hemolysis were less in the EASs ($p<0.001$). The ammonia levels were higher in all the EASs than in Adsol, with the exception of EAS 46. During storage, the extracorpuscular and intracorpuscular pH levels were essentially identical. The shedding of microvesicles was greatly reduced in all the EASs.

CONCLUSION: Cell swelling induced in RBCs after collection appears to improve preservation. Ammonia and phosphate enhance RBC ATP maintenance. Glycine decreases the formation of ammonia by RBCs stored in a hypotonic medium.

Identifiers--KeyWord Plus(R): AMINO-ACID-TRANSPORT; HUMAN-ERYTHROCYTES; KCL COTRANSPORT; MEMBRANE VESICULATION; STORED ERYTHROCYTES; ADDITIVE SOLUTION; CL COTRANSPORT; BLOOD-CELLS; RAT-LIVER; VOLUME

Research Fronts: 95-3190 001 (INCREASED ABUNDANCE OF SPECIFIC SKELETAL-MUSCLE PROTEIN-TYROSINE PHOSPHATASES; ALPHA-B- **CRYSTALLIN** EXPRESSION)

95-3483 001 (MULTIDRUG-RESISTANCE P-GLYCOPROTEIN; CELL VOLUME-ACTIVATED **CHLORIDE** CHANNELS; EXPRESSION PATTERN)

95-5062 001 (L- **ARGININE** TRANSPORT; NITRIC-OXIDE SYNTHASE ACTIVITY; SYSTEM Y(+))

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...Abstract: in hypo-osmolar additive solutions with the same concentrations of adenine, dextrose, mannitol, and sodium **chloride** and varied amounts of ammonium, phosphate, glycerol, and glutamine were better preserved than RBCs in...
...solutions (EASs) all containing adenine, 2 mM; dextrose, 110 mM; mannitol, 55 mM; and sodium **chloride** , 50 mM. EAS 42 had, in addition, glutamine, 10 mM; glycine 5 mM; and phosphate...
Research Fronts: 95-3190 001 (INCREASED ABUNDANCE OF SPECIFIC SKELETAL-MUSCLE PROTEIN-TYROSINE PHOSPHATASES; ALPHA-B- **CRYSTALLIN** EXPRESSION)
95-3483 001 (MULTIDRUG-RESISTANCE P-GLYCOPROTEIN; CELL VOLUME-ACTIVATED **CHLORIDE** CHANNELS; EXPRESSION PATTERN)
95-5062 001 (L- **ARGININE** TRANSPORT; NITRIC-OXIDE SYNTHASE ACTIVITY; SYSTEM Y(+))

5/9,K/5 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05533867 Genuine Article#: WE933 Number of References: 41
Title: Inactivation and recovery of nitric oxide synthetic capability in cytokine-induced RAW 264.7 cells treated with ''irreversible'' NO synthase inhibitors
Author(s): Wolff DJ (REPRINT) ; Lubeskie A; Li C
Corporate Source: UNIV MED & DENT NEW JERSEY,ROBERT WOOD JOHNSON MED SCH, DEPT PHARMACOL/PISCATAWAY//NJ/08854 (REPRINT)
Journal: ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS, 1997, V338, N1 (FEB 1), P

73-82
ISSN: 0003-9861 Publication date: 19970201
Publisher: ACADEMIC PRESS INC JNL-COMP SUBSCRIPTIONS, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495
Language: English Document Type: ARTICLE
Geographic Location: USA
Subfile: CC LIFE--Current Contents, Life Sciences
Journal Subject Category: BIOCHEMISTRY & MOLECULAR BIOLOGY; BIOPHYSICS
Abstract: As measured at 100 mu M extracellular **arginine** , aminoguanidine produced a time- and concentration-dependent inactivation of nitric oxide (NO) synthesis by cytokine-induced RAW cells, Inactivation obeyed first-order kinetics and occurred at a maximal rate of 0.22 min(-1) with a half-maximal inactivation rate observed at a concentration of 670 mu M aminoguanidine (K-I value). Inactivation of NO synthetic activity in the presence of N-G-methyl-L- **arginine** similarly followed first-order kinetics with a maximal inactivation rate of 0.07 min(-1) and a K-I value of 170 mu M. Inactivation of NO synthetic activity in the presence of diphenyliodonium **chloride** occurred with a maximal inactivation rate of 0.24 min(-1) with a K-I value of 14 mu M. Diphenyliodonium **chloride** also produced a first-order rate of inactivation of cytokine-inducible nitric oxide synthase (iNOS) activity affinity purified from cytokine-induced RAW cells with a maximal inactivation rate of its cytochrome c reductase activity of 0.24 min(-1) with a K-I value of 18 mu M. Cytokine-induced RAW cells were treated with aminoguanidine, N-G-methyl-L- **arginine** , and diphenyliodonium **chloride** at concentrations and for a time sufficient to completely inactivate NO synthesis by the cells and were allowed torecover in drug-free medium. Despite the presence of cycloheximide, NO synthetic rate recovered from 70 to 90% of its pretreatment activity over 4 h in cells exposed to either aminoguanidine or N-G-methyl-L-arsnine but did not recover from exposure to diphenyliodonium **chloride** . Analysis by sucrose density gradient centrifugation of the cytochrome c reductase and citrulline-forming activities in extracts of cells recovered from aminoguanidine treatment revealed that recovery was accompa nied by a diminished population of iNOS monomers with an increased population of iNOS dimers. This observation is consistent with the hypothesis that for the mechanism-based inactivator aminoguanidine, functional dimers can be assembled from ''drug-undamaged'' monomers during the recovery period. (C) 1997 Academic Press.
Descriptors--Author Keywords: aminoguanidine ; N-G-methyl-L- **arginine** ; diphenyliodonium **chloride** ; nitric oxide synthesis ; mechanism-based inactivation ; recovery ; intact cells
Identifiers--KeyWord Plus(R): METHYL-L- **ARGININE** ; IN-VIVO; AMINOGUANIDINE; MACROPHAGE; MECHANISM; DIPHENYLENEIODONIUM; IMIDAZOLE; REDUCTASE; ENZYME; POLYPEPTIDE
Research Fronts: 95-0388 003 (NITRIC-OXIDE SYNTHASE; ALDEHYDE FIXATION DIFFERENTIALLY AFFECTS DISTRIBUTION OF DIAPHORASE ACTIVITY; LIGHT-INDUCED FOS EXPRESSION)
95-1748 002 (INDUCIBLE NITRIC-OXIDE SYNTHASE; IN-VITRO ENDOTOXIN EXPOSURE INDUCES CONTRACTILE DYSFUNCTION IN ADULT-RAT CARDIAC MYOCYTES)
95-2212 001 (PEROXYNITRITE IN-VITRO; NITRIC-OXIDE SYNTHASE; HYDROXYL RADICAL; FORMATION OF 8-NITROGUANINE; PC12 CELLS)
95-3190 001 (INCREASED ABUNDANCE OF SPECIFIC SKELETAL-MUSCLE PROTEIN-TYROSINE PHOSPHATASES; ALPHA-B- **CRYSTALLIN** EXPRESSION)
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Abstract: As measured at 100 mu M extracellular **arginine** , aminoguanidine produced a time- and concentration-dependent inactivation of nitric oxide (NO) synthesis by cytokine...

...I value). Inactivation of NO synthetic activity in the presence of N-G-methyl-L- **arginine** similarly followed first-order kinetics with a maximal inactivation rate of 0.07 min(-1...

...value of 170 mu M. Inactivation of NO synthetic activity in the presence of diphenyliodonium **chloride** occurred with a maximal inactivation rate of 0.24 min(-1) with a K-I value of 14 mu M. Diphenyliodonium **chloride** also produced a first-order rate of inactivation of cytokine-inducible nitric oxide synthase (iNOS...

...18 mu M. Cytokine-induced RAW cells were treated with aminoguanidine, N-G-methyl-L- **arginine** , and diphenyliodonium **chloride** at concentrations and for a time sufficient to completely inactivate NO

synthesis by the cells...

...aminoguanidine or N-G-methyl-L-arsnine but did not recover from exposure to diphenyliodonium **chloride** . Analysis by sucrose density gradient centrifugation of the cytochrome c reductase and citrulline-forming activities...
...Identifiers--METHYL-L- **ARGININE** ; IN-VIVO; AMINOGUANIDINE; MACROPHAGE; MECHANISM; DIPHENYLENEIODONIUM; IMIDAZOLE; REDUCTASE; ENZYME; POLYPEPTIDE
...Research Fronts: CELLS)
95-3190 001 (INCREASED ABUNDANCE OF SPECIFIC SKELETAL-MUSCLE PROTEIN-TYROSINE PHOSPHATASES; ALPHA-B- **CRYSTALLIN** EXPRESSION)

5/9,K/6 (Item 6 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05463541 Genuine Article#: WA564 Number of References: 51
Title: EXPRESSION OF THE CYSTIC-FIBROSIS PHENOTYPE IN A RENAL AMPHIBIAN EPITHELIAL-CELL LINE
Author(s): LING BN; ZUCKERMAN JB; LIN CM; HARTE BJ; MCNULTY KA; SMITH PR; GOMEZ LM; WORRELL RT; EATON DC; KLEYMAN TR
Corporate Source: DEPT VET AFFAIRS,MED CTR,UNIV & WOODLAND AVE/PHILADELPHIA//PA/19104; DEPT VET AFFAIRS,MED CTR/PHILADELPHIA//PA/19104; DEPT VET AFFAIRS MED CTR/ATLANTA//GA/30322; EMORY UNIV,DIV RENAL/ATLANTA//GA/30322; EMORY UNIV,DEPT MED/ATLANTA//GA/30322; EMORY UNIV,DEPT PHYSIOL/ATLANTA//GA/30322; EMORY UNIV,CTR CELL & MOL SIGNALING/ATLANTA//GA/30322; UNIV PENN,DEPT MED/PHILADELPHIA//PA/19104; UNIV PENN,DEPT PHYSIOL/PHILADELPHIA//PA/19104; ALLEGHENY UNIV HLTH SCI,DEPT PHYSIOL/PHILADELPHIA//PA/19129
Journal: JOURNAL OF BIOLOGICAL CHEMISTRY, 1997, V272, N1 (JAN 3), P594-600
ISSN: 0021-9258
Language: ENGLISH Document Type: ARTICLE
Geographic Location: USA
Subfile: Science Citation Index; SciSearch; CC LIFE--Current Contents, Life Sciences
Journal Subject Category: BIOCHEMISTRY & MOLECULAR BIOLOGY
Abstract: Mutations in a Cl- channel (cystic fibrosis transmembrane conductance regulator or CFTR) are responsible for the cystic fibrosis (CF) phenotype, Increased Na+ transport rates are observed in CF airway epithelium, and recent studies suggest that this is due to an increase in Na+ channel open probability (P-o), The Xenopus renal epithelial cell line, A6, expresses both cAMP-activated 8-picosiemen (pS) Cl- channels and amiloride-sensitive 4-pS Na+ channels, and provides a model system for examining the interactions of CFTR and epithelial Na+ channels, A6 cells express CFTR mRNA, as demonstrated by reverse transcriptase-polymerase chain reaction and partial sequence analysis, A phosphorothioate antisense oligonucleotide, complementary to the 5' end of the open reading frame of Xenopus CFTR, was used to inhibit functional expression of CFTR in A6 cells, Parallel studies utilized the corresponding sense oligonucleotide as a control, CFTR protein expression was markedly reduced in cells incubated with the antisense oligonucleotide. Incubation of A6 cells with the antisense oligonucleotide led to inhibition of forskolin-activated amiloride-insensitive short circuit current (I-sc), After a 30-min

exposure to 10 mu M forskolin, 8-pS Cl- channel activity was detected in only 1 of 31 (3%) cell-attached patches on cells treated with antisense oligonucleotide, compared to 5 of 19 (26%) patches from control cells, A shift in the single-channel current-voltage relationship derived from antisense-treated cells was also consistent with a reduction in Cl- reabsorption, Both amiloride-sensitive I-sc and Na+ channel P-o were significantly increased in antisense-treated, forskolin-stimulated A6 cells, when compared with forskolin-stimulated controls, These data suggest that the regulation of Na+ channels by CFTR is not limited to respiratory epithelia and to epithelial cells in culture overexpressing CFTR and epithelial Na+ channels.

Identifiers--KeyWords Plus: TRANSMEMBRANE CONDUCTANCE REGULATOR; PROTEIN-KINASE-C; NA+ CHANNELS; SODIUM-CHANNELS; **CHLORIDE** CHANNELS; ANTISENSE OLIGODEOXYNUCLEOTIDE; **ARGININE** -VASOPRESSIN; AIRWAY EPITHELIA; CFTR; A6

Research Fronts: 95-0327 004 (CYSTIC-FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR GENE; DIETARY-CHANGES IMPROVE SURVIVAL OF CFTR S489X HOMOZYGOUS MUTANT MOUSE)

95-5061 002 (STRUCTURAL GENE; GLTC-DEPENDENT REGULATION OF BACILLUS-SUBTILIS GLUTAMATE SYNTHASE EXPRESSION; ARABIDOPSIS TYPE-1 PROTEIN PHOSPHATASE)

95-3190 001 (INCREASED ABUNDANCE OF SPECIFIC SKELETAL-MUSCLE PROTEIN-TYROSINE PHOSPHATASES; ALPHA-B- **CRYSTALLIN** EXPRESSION)

95-4481 001 (K+ CHANNELS IN CULTURED RAT NEURONAL CELLS; DIFFERENT GATING KINETICS; SINGLE NMDA RECEPTOR CURRENTS; CARDIAC SARCOPLASMIC-RETICULUM)

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...Identifiers--TRANSMEMBRANE CONDUCTANCE REGULATOR; PROTEIN-KINASE-C; NA+ CHANNELS; SODIUM-CHANNELS; **CHLORIDE** CHANNELS; ANTISENSE OLIGODEOXYNUCLEOTIDE; **ARGININE** -VASOPRESSIN; AIRWAY EPITHELIA; CFTR; A6
...Research Fronts: PHOSPHATASE)
95-3190 001 (INCREASED ABUNDANCE OF SPECIFIC SKELETAL-MUSCLE PROTEIN-TYROSINE PHOSPHATASES; ALPHA-B- **CRYSTALLIN** EXPRESSION)
95-4481 001 (K+ CHANNELS IN CULTURED RAT NEURONAL CELLS; DIFFERENT GATING KINETICS; SINGLE...

5/9,K/7 (Item 7 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05457800 Genuine Article#: WA251 Number of References: 31
Title: AMYLIN AND FOOD-INTAKE IN MICE - EFFECTS ON MOTIVATION TO EAT AND MECHANISM OF ACTION
Author(s): MORLEY JE; SUAREZ MD; MATTAMAL M; FLOOD JF
Corporate Source: ST LOUIS UNIV,SCH MED M239,DIV GERIATR MED,1402S GRAND BLVD/ST LOUIS//MO/63104; VET ADM MED CTR,CTR GERIATR RES EDUC & CLIN/ST LOUIS//MO/63106
Journal: PHARMACOLOGY BIOCHEMISTRY AND BEHAVIOR, 1997, V56, N1 (JAN), P 123-129
ISSN: 0091-3057
Language: ENGLISH Document Type: ARTICLE
Geographic Location: USA
Subfile: Science Citation Index; SciSearch; CC LIFE--Current Contents, Life Sciences
Journal Subject Category: PHARMACOLOGY & PHARMACY
Abstract: Amylin is a hormone produced by the pancreatic islets of Langerhans. Amylin decreased food pellet consumption. Amylin also decreased lever pressing for milk solution whether or not the mice were prefed. Amylin did not produce a conditioned taste aversion in a two bottle test, whereas lithium **chloride** did. In addition, L- **arginine** ,

a precursor for nitric oxide synthesis, was demonstrated to inhibit the ability of amylin to decrease food intake. Amylin did not alter nitric oxide synthase activity in the fundus of the stomach. These studies demonstrated that amylin inhibits food intake at a higher range of doses than is typical of anorectic agents such as cholecystokinin. Amylin does not appear to decrease food intake by reducing the release of nitric oxide but may affect appetite by modulating serum glucose levels when co-released with insulin. Copyright (C) 1997 Elsevier

Science Inc.

Descriptors--Author Keywords: AMYLIN ; APPETITE ; FOOD INTAKE ; NITRIC OXIDE ; L- **ARGININE** ; NITRIC OXIDE SYNTHASE ; LEVER PRESS ; ANOREXIA ; MOTIVATION

Identifiers--KeyWords Plus: GUT PEPTIDES; RATS; SATIETY; MODULATION; INJECTION; APPETITE; WEIGHT

Research Fronts: 95-3190 001 (INCREASED ABUNDANCE OF SPECIFIC SKELETAL-MUSCLE PROTEIN-TYROSINE PHOSPHATASES; ALPHA-B- **CRYSTALLIN** EXPRESSION)

95-4861 001 (LICKING BEHAVIOR IN RATS; GASTRIN-RELEASING PEPTIDE; INGESTIVE TASTE REACTIVITY)

95-8036 001 (OBESE ZUCKER RATS; CENTRAL INSULIN; HYPOTHALAMIC PARAVENTRICULAR NUCLEUS; INVOLVEMENT OF NEUROPEPTIDE-Y; OPIOID ANTAGONIST NALOXONE)

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...Abstract: Amylin did not produce a conditioned taste aversion in a two

bottle test, whereas lithium **chloride** did. In addition, L- **arginine** , a precursor for nitric oxide synthesis, was demonstrated to inhibit the ability of amylin to...
Research Fronts: 95-3190 001 (INCREASED ABUNDANCE OF SPECIFIC SKELETAL-MUSCLE PROTEIN-TYROSINE PHOSPHATASES; ALPHA-B- **CRYSTALLIN** EXPRESSION)
95-4861 001 (LICKING BEHAVIOR IN RATS; GASTRIN-RELEASING PEPTIDE; INGESTIVE TASTE REACTIVITY)
95...

5/9,K/8 (Item 8 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

00857477 Genuine Article#: FC075 Number of References: 22
Title: INTERACTIONS BETWEEN ION-EXCHANGE AND METABOLISM IN ERYTHROCYTES OF THE RAINBOW-TROUT ONCORHYNCHUS-MYKISS
Author(s): TUFTS BL; BOUTILIER RG
Corporate Source: DALHOUSIE UNIV,DEPT BIOL/HALIFAX B3H 4J1/NS/CANADA/
Journal: JOURNAL OF EXPERIMENTAL BIOLOGY, 1991, V156, MAR, P139-151
Language: ENGLISH Document Type: ARTICLE
Geographic Location: CANADA
Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences; CC AGRI--

Current Contents, Agriculture, Biology & Environmental Sciences
Journal Subject Category: BIOLOGY
Abstract: Experiments were carried out to investigate the relationship between ion exchange and energy metabolism in rainbow trout erythrocytes in vitro. Under resting conditions, the sodium/potassium pump accounts for 20% of the cellular energy budget. In the presence of the beta-adrenergic agonist isoproterenol, however, this increases to 43%. Inhibition of the sodium/potassium pump with ouabain results in greater increases in erythrocyte water content and sodium and **chloride** concentrations and a greater decrease in erythrocyte potassium concentration following stimulation by isoproterenol. Moreover, the decrease in erythrocyte NTP levels observed following adrenergic stimulation does not occur when the sodium/potassium pump is inhibited with ouabain. Inhibition of the sodium/potassium pump also abolishes the increase in oxygen consumption by the cells which normally takes place following adrenergic stimulation. Finally, depletion of erythrocyte NTP levels by the sodium ionophore monensin or by previous incubation with nitrogen does not result in a significant increase in oxygen consumption. Thus, catecholamines appear to be crucial for the metabolic-membrane coupling that occurs following adrenergic stimulation in rainbow trout erythrocytes.
Descriptors--Author Keywords: ERYTHROCYTES; TROUT; ION EXCHANGE; METABOLISM; ONCORHYNCHUS-MYKISS
Identifiers--KeyWords Plus: RED-CELLS; PROTEIN-PHOSPHORYLATION; ADRENERGIC-STIMULATION; FISH ERYTHROCYTES; HORMONAL-CONTROL; PH REGULATION; MEMBRANE; TRANSPORT; VOLUME; INVIVO
Research Fronts: 89-1358 001 (RAINBOW-TROUT (SALMO-GAIRDNERI); ACID-BASE REGULATION FOLLOWING EXHAUSTIVE EXERCISE; MARINE FISH; RESPIRATORY ADAPTATIONS; ENZYMES OF **ARGININE** METABOLISM)
89-4150 001 (PHOSPHORYLATION OF PROTEINS; CATALYTIC SUBUNIT; GLYCOGEN-SYNTHASE ACTIVITY; CASEIN KINASE-2; LENS ALPHA- **CRYSTALLIN** A-CHAIN; PHOSPHODIESTER LINKAGE)

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...Abstract: potassium pump with ouabain results in greater increases in erythrocyte water content and sodium and **chloride** concentrations and a greater decrease in erythrocyte potassium concentration following stimulation by isoproterenol. Moreover, the...
...Research Fronts: TROUT (SALMO-GAIRDNERI); ACID-BASE REGULATION FOLLOWING EXHAUSTIVE EXERCISE; MARINE FISH; RESPIRATORY ADAPTATIONS; ENZYMES OF **ARGININE** METABOLISM)
89-4150 001 (PHOSPHORYLATION OF PROTEINS; CATALYTIC SUBUNIT; GLYCOGEN-SYNTHASE ACTIVITY; CASEIN KINASE-2; LENS ALPHA- **CRYSTALLIN** A-CHAIN; PHOSPHODIESTER LINKAGE)

5/9,K/9 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

13167229 EMBASE No: 2005234088
Alexander-disease mutation of GFAP causes filament disorganization and decreased solubility of GFAP
Hsiao V.C.; Tian R.; Long H.; Perng M.D.; Brenner M.; Quinlan R.A.; Goldman J.E.
J.E. Goldman, Department of Pathology, Center for Neurobiology and Behavior, Columbia University, New York, NY 10032 United States
AUTHOR EMAIL: jeg5@columbia.edu
Journal of Cell Science (J. CELL SCI.) (United Kingdom) 01 MAY 2005, 118/9 (2057-2065)
CODEN: JNCSA ISSN: 0021-9533
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 66

Alexander disease is a fatal neurological illness characterized by white-matter degeneration and the formation of astrocytic cytoplasmic inclusions called Rosenthal fibers, which contain the intermediate filament

glial fibrillary acidic protein (GFAP), the small heat-shock proteins HSP27 and alphaB- **crystallin** , and ubiquitin. Many Alexander-disease patients are heterozygous for one of a set of point mutations in the GFAP gene, all of which result in amino acid substitutions. The biological effects of the most common alteration, R239C, were tested by expressing the mutated protein in cultured cells by transient transfection. In primary rat astrocytes and Cos-7 cells, the mutant GFAP was incorporated into filament networks along with the endogenous GFAP and vimentin, respectively. In SW13VimSUP- cells, which have no endogenous cytoplasmic intermediate filaments, wild-type human GFAP frequently formed filamentous bundles, whereas the R239C GFAP formed 'diffuse' and irregular patterns. Filamentous bundles of R239C GFAP were sometimes formed in SW13VimSUP- cells when wild-type GFAP was co-transfected. Although the presence of a suitable coassembly partner (vimentin or GFAP) reduced the potential negative effects of the R239C mutation on GFAP network formation, the mutation affected the stability of GFAP in cells in a dominant fashion. Extraction of transfected SW13VimSUP- cells with Triton-X-100-containing buffers showed that the mutant GFAP was more resistant to solubilization at elevated KCl concentrations. Both wild-type and R239C GFAP assembled into 10 nm filaments with similar morphology in vitro. Thus, although the R239C mutation does not appear to affect filament formation per se, the mutation alters the normal solubility and organization of GFAP networks.

DRUG DESCRIPTORS:
*glial fibrillary acidic protein--endogenous compound--ec
heat shock protein 27--endogenous compound--ec; alpha **crystallin** --endogenous compound--ec; beta **crystallin** --endogenous compound--ec; ubiquitin--endogenous compound--ec; amino acid--endogenous compound--ec; mutant protein--endogenous compound--ec; vimentin--endogenous compound--ec; triton x 100; buffer; potassium **chloride** ; **arginine** --endogenous compound --ec; cysteine--endogenous compound--ec
MEDICAL DESCRIPTORS:
*Alexander disease--diagnosis--di; *Alexander disease--etiology--et gene mutation; neurologic disease--etiology--et; clinical feature; white matter; astrocyte; cell inclusion; heterozygosity; point mutation; amino acid substitution; protein expression; cell culture; genetic transfection; cytoplasm; wild type; protein assembly; intermediate filament; protein stability; solubilization; concentration (parameters); cell structure; in vitro study; protein structure; human; nonhuman; rat; controlled study; human cell; animal cell; article; priority journal
CAS REGISTRY NO.: 60267-61-0 (ubiquitin); 65072-01-7 (amino acid); 7447-40-7 (potassium **chloride**); 1119-34-2, 15595-35-4, 7004-12-8, 74-79-3 (**arginine**); 4371-52-2, 52-89-1, 52-90-4 (cysteine)
SECTION HEADINGS:
005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
022 Human Genetics
029 Clinical and Experimental Biochemistry

...intermediate filament glial fibrillary acidic protein (GFAP), the small heat-shock proteins HSP27 and alphaB- **crystallin** , and ubiquitin. Many Alexander-disease patients are heterozygous for one of a set of point
...
DRUG DESCRIPTORS:
heat shock protein 27--endogenous compound--ec; alpha **crystallin** --endogenous compound--ec; beta **crystallin** --endogenous compound--ec; ubiquitin--endogenous compound--ec; amino acid--endogenous compound--ec;

mutant protein--endogenous compound--ec; vimentin--endogenous compound--ec; triton x 100; buffer; potassium **chloride** ; **arginine** --endogenous compound --ec; cysteine--endogenous compound--ec
CAS REGISTRY NO.: 60267-61-0 (ubiquitin); 65072-01-7 (amino acid); 7447-40-7 (potassium **chloride**); 1119-34-2...

...74-79-3 (**arginine**); 4371-52-2...

5/9,K/10 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

07461271 EMBASE No: 1998370560
Human procarboxypeptidase U, or thrombin-activable fibrinolysis inhibitor, is a substrate for transglutaminases: Evidence for transglutaminase-catalyzed cross-linking to fibrin
Valnickova Z.; Enghild J.J.
J.J. Enghild, Box 3712, Duke University Medical Center, Durham, NC 27710 United States
AUTHOR EMAIL: enghi001@mc.duke.edu
Journal of Biological Chemistry (J. BIOL. CHEM.) (United States) 16 OCT 1998, 273/42 (27220-27224)
CODEN: JBCHA ISSN: 0021-9258
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 45

Procarboxypeptidase U (EC 3.4.17.20) (pro-CpU), also known as plasma procarboxypeptidase B and thrombin-activable fibrinolysis inhibitor, is a human plasma protein that has been implicated in the regulation of fibrinolysis. In this study, we show that pro-CpU serves as a substrate for transglutaminases. Both factor XIIIa and tissue transglutaminase catalyzed the polymerization of pro-CpU and the cross-linking to fibrin as well as the incorporation of 5-dimethylaminonaphthalene-1-sulfonyl cadaverine (dansylcadaverine), [sup 1sup 4C]putrescine, and dansyl-PGGQQIV. These findings show that pro-CpU contains both amine acceptor (Gln) and amine donor (Lys) residues. The amine acceptor residues were identified as Glnsup 2, Glnsup 5, and Glnsup 2sup 9sup 2, suggesting that both the activation peptide and the mature enzyme participate in the cross-linking reaction. These observations imply that transglutaminases may mediate covalent binding of pro-CpU to other proteins and cell surfaces in vivo. In particular, factor XIIIa may cross-link pro- CpU to fibrin during the latter part of the coagulation cascade, thereby helping protect the newly formed fibrin clot from premature plasmin degradation. Moreover, the cross-linking may facilitate the activation of pro-CpU, stabilize the enzymatic activity, and protect the active enzyme from further degradation.

DRUG DESCRIPTORS:
*protein glutamine gamma glutamyltransferase--endogenous compound--ec; * antifibrinolytic agent--endogenous compound--ec
dansylcadaverine--endogenous compound--ec; putrescine--endogenous compound --ec; dansyl **chloride** --endogenous compound--ec; glutamine--endogenous compound--ec; lysine--endogenous compound--ec; blood clotting factor 13 --endogenous compound--ec; fibrin--endogenous compound--ec; plasmin --endogenous compound--ec; **arginine** --endogenous compound--ec; alpha 2 antiplasmin--endogenous compound--ec; amine--endogenous compound--ec;

plasminogen activator inhibitor 1--endogenous compound--ec; beta **crystallin** --endogenous compound--ec; fibrinogen--endogenous compound--ec; vitronectin--endogenous compound--ec; unclassified drug
MEDICAL DESCRIPTORS:
*fibrinolysis; *enzyme substrate
fibrin polymerization; covalent bond; fibrin clot; enzyme activity; enzyme stability; enzyme degradation; liver; sequence homology; carboxy terminal sequence; enzyme active site; protein cross linking; enzyme specificity; human; nonhuman; human tissue; animal tissue; article; priority journal
DRUG TERMS (UNCONTROLLED): procarboxypapetidase u--endogenous compound--ec; thrombin activable fibrinolysis inhibitor
CAS REGISTRY NO.: 80146-85-6 (protein glutamine gamma glutamyltransferase); 10121-91-2 (dansylcadaverine); 110-60-1, 333-93-7 (putrescine); 605-65-2 (dansyl **chloride**); 56-85-9, 6899-04-3 (glutamine); 56-87-1, 6899-06-5, 70-54-2 (lysine); 9013-56-3 (blood clotting factor 13); 9001-31-4 (fibrin); 9001-90-5, 9004-09-5 (plasmin); 1119-34-2, 15595-35-4, 7004-12-8, 74-79-3 (**arginine**); 140208-23-7 (plasminogen activator inhibitor 1); 9001-32-5 (fibrinogen)
SECTION HEADINGS:
025 Hematology
029 Clinical and Experimental Biochemistry
DRUG DESCRIPTORS:
dansylcadaverine--endogenous compound--ec; putrescine--endogenous compound --ec; dansyl **chloride** --endogenous compound--ec; glutamine--endogenous compound--ec; lysine--endogenous compound--ec; blood clotting factor 13 --endogenous compound--ec; fibrin--endogenous compound--ec; plasmin --endogenous compound--ec; **arginine** --endogenous compound--ec; alpha 2 antiplasmin--endogenous compound--ec; amine--endogenous compound--ec; plasminogen activator inhibitor 1--endogenous compound--ec; beta **crystallin** --endogenous compound--ec; fibrinogen--endogenous compound--ec; vitronectin--endogenous compound--ec; unclassified drug
...CAS REGISTRY NO.: 333-93-7 (putrescine); 605-65-2 (dansyl **chloride**); 56-85-9...

...74-79-3 (**arginine**); 140208-23-7 (plasminogen activator inhibitor 1); 9001-32-5 (fibrinogen)
? s arginine(n)hydrochloride
416125 ARGININE
382785 HYDROCHLORIDE
S6 942 ARGININE(N)HYDROCHLORIDE
? s s1 and s6
40380 S1
942 S6
S7 10 S1 AND S6
? t s7/9,k/all

7/9,K/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0015321550 BIOSIS NO.: 200510016050
Arginine hydrochloride **enhances the dynamics of subunit assembly and the chaperone-like activity of alpha-** crystallin
AUTHOR: Srinivas V; Raman B; Rao K Sridhar; Ramakrishna T; Rao Ch Mohan (Reprint)
AUTHOR ADDRESS: Ctr Cellular and Mol Biol, Uppal Rd, Hyderabad 500007, Andhra Pradesh, India**India

AUTHOR E-MAIL ADDRESS: mohan@ccmb.res.in
JOURNAL: Molecular Vision 11 (27-29): p249-255 APR 1 05 2005
ISSN: 1090-0535
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Purpose: alpha- **Crystallin** , a major eye lens protein, bears homology with small heat shock proteins (sHsps) and exhibits molecular chaperone-like activity. Structural perturbation by temperature or low concentrations of denaturants leads to enhancement of its chaperone-like activity. We have earlier demonstrated similar enhancement of chaperone-like activity using biologically compatible solutes such as **arginine hydrochloride** and aminoguanidine. The purpose of the present study is to get an insight into the mechanism of the arginine induced enhancement of chaperone-like activity of alpha- **crystallin** .Methods: The effect of **arginine hydrochloride** on the chaperone-like activity of alpha- **crystallin** at 25 degrees C was studied using DTT induced aggregation of insulin as a model system. Changes in the accessibility of the thiol group near the end of the alpha- **crystallin** domain in the absence and the presence of **arginine hydrochloride** were studied using dithiobisnitrobenzoic acid. Fluorescence resonance energy transfer studies were performed to investigate changes in the dynamics of the subunit assembly. Urea induced denaturation studies of alpha- **crystallin** were carried out to investigate structural destabilization of alpha- **crystallin** , if any, in the presence of **arginine hydrochloride** .Results: **Arginine hydrochloride** increases the chaperone-like activity of alpha- **crystallin** several fold towards DTT induced aggregation of insulin at room temperature. Our study shows that both the extent and the rate of accessibility of the thiol group are increased in the presence of arginine. Fluorescence resonance energy transfer experiments show that **arginine hydrochloride** significantly increases the subunit exchange between the oligomers of alpha- **crystallin** . Arginine induced structural perturbation and loosening of subunit assembly of alpha- **crystallin** leads to overall destabilization of the protein as reflected by the urea denaturation study.Conclusions: Arginine perturbs the tertiary and quaternary structure of alpha- **crystallin** and enhances the dynamics of the subunit assembly leading to enhanced chaperone-like activity. Thus, in addition to size, surface hydrophobicity, and charge distribution, the dynamics of the subunit assembly appears to be one of the critical factors that can modulate the chaperone activity.

REGISTRY NUMBERS: 9004-10-8: insulin; 79-17-4: aminoguanidine; 32042-43-6: **arginine hydrochloride**
DESCRIPTORS:
MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Sense Organs--Sensory Reception
ORGANISMS: PARTS ETC: eye lens
CHEMICALS & BIOCHEMICALS: insulin; small heat shock proteins; aminoguanidine; **arginine hydrochloride** ; alpha- **crystallin** -- chaperone-like activity
CONCEPT CODES:
10060 Biochemistry studies - General
10064 Biochemistry studies - Proteins, peptides and amino acids
20004 Sense organs - Physiology and biochemistry

Arginine hydrochloride **enhances the dynamics of subunit assembly and the chaperone-like activity of alpha-** crystallin

ABSTRACT: Purpose: alpha- **Crystallin** , a major eye lens protein, bears homology with small heat shock proteins (sHsps) and exhibits...

...have earlier demonstrated similar enhancement of chaperone-like activity using biologically compatible solutes such as **arginine hydrochloride** and aminoguanidine. The purpose of the present study is to get an insight into the mechanism of the arginine induced enhancement of chaperone-like activity of alpha- **crystallin** .Methods: The effect of **arginine hydrochloride** on the chaperone-like activity of alpha- **crystallin** at 25 degrees C was studied using DTT induced aggregation of insulin as a model system. Changes in the accessibility of the thiol group near the end of the alpha- **crystallin** domain in the absence and the presence of **arginine hydrochloride** were studied using dithiobisnitrobenzoic acid. Fluorescence resonance energy transfer studies were performed to investigate changes in the dynamics of the subunit assembly. Urea induced denaturation studies of alpha- **crystallin** were carried out to investigate structural destabilization of alpha- **crystallin** , if any, in the presence of **arginine hydrochloride** .Results: **Arginine hydrochloride** increases the chaperone-like activity of alpha- **crystallin** several fold towards DTT induced aggregation of insulin at room temperature. Our study shows that...

...group are increased in the presence of arginine. Fluorescence resonance energy transfer experiments show that **arginine hydrochloride** significantly increases the subunit exchange between the oligomers of alpha- **crystallin** . Arginine induced structural perturbation and loosening of subunit assembly of alpha- **crystallin** leads to overall destabilization of the protein as reflected by the urea denaturation study.Conclusions: Arginine perturbs the tertiary and quaternary structure of alpha- **crystallin** and enhances the dynamics of the subunit assembly leading to enhanced chaperone-like activity. Thus...
...REGISTRY NUMBERS: **arginine hydrochloride**
DESCRIPTORS:
CHEMICALS & BIOCHEMICALS: ... **arginine hydrochloride** ; ...

...alpha- **crystallin** --

7/9,K/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014361712 BIOSIS NO.: 200300320431
Structural perturbation and enhancement of the chaperone-like activity of alpha- crystallin **by** arginine hydrochloride .
AUTHOR: Srinivas Volety; Raman Bakthisaran; Rao Kunchala Sridhar; Ramakrishna Tangirala; Rao Ch Mohan (Reprint)
AUTHOR ADDRESS: Centre for Cellular and Molecular Biology, Uppal Road, Hyderabad, 500 007, India**India
AUTHOR E-MAIL ADDRESS: mohan@ccmb.res.in
JOURNAL: Protein Science 12 (6): p1262-1270 June 2003 2003
MEDIUM: print
ISSN: 0961-8368
DOCUMENT TYPE: Article

RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Structural perturbation of alpha- **crystallin** is shown to enhance its molecular chaperone-like activity in preventing aggregation of target proteins. We demonstrate that arginine, a biologically compatible molecule that is known to bind to the peptide backbone and negatively charged side-chains, increases the chaperone-like activity of calf eye lens alpha- **crystallin** as well as recombinant human alphaA- and alphaB-crystallins. Arginine-induced increase in the chaperone activity is more pronounced for alphaB- **crystallin** than for alphaA- **crystallin** . Other guanidinium compounds such as aminoguanidine hydrochloride and guanidine hydrochloride also show a similar effect, but to different extents. A point mutation, R120G, in alphaB- **crystallin** that is associated with desmin-related myopathy, results in a significant loss of chaperone-like activity. Arginine restores the activity of mutant protein to a considerable extent. We have investigated the effect of arginine on the structural changes of alpha- **crystallin** by circular dichroism, fluorescence, and glycerol gradient sedimentation. Far-UV CD spectra show no significant changes in secondary structure, whereas near-UV CD spectra show subtle changes in the presence of arginine. Glycerol gradient sedimentation shows a significant decrease in the size of alpha- **crystallin** oligomer in the presence of arginine. Increased exposure of hydrophobic surfaces of alpha- **crystallin** , as monitored by pyrene-solubilization and ANS-fluorescence, is observed in the presence of arginine. These results show that arginine brings about subtle changes in the tertiary structure and significant changes in the quaternary structure of alpha- **crystallin** and enhances its chaperone-like activity significantly. This study should prove useful in designing strategies to improve chaperone function for therapeutic applications.

REGISTRY NUMBERS: 1119-34-2Q: **arginine hydrochloride** ; 15595-35-4Q: **arginine hydrochloride** ; 32042-43-6Q: **arginine hydrochloride** ; 1937-19-5Q: aminoguanidine hydrochloride; 16139-18-7Q: aminoguanidine hydrochloride

DESCRIPTORS:

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics

BIOSYSTEMATIC NAMES: Bovidae--Artiodactyla, Mammalia, Vertebrata, Chordata, Animalia; Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGANISMS: cow (Bovidae); human (Hominidae)

ORGANISMS: PARTS ETC: lens--sensory system

COMMON TAXONOMIC TERMS: Artiodactyls; Nonhuman Vertebrates; Nonhuman Mammals; Animals; Chordates; Humans; Mammals; Primates; Vertebrates

DISEASES: desmin-related myopathy--muscle disease

CHEMICALS & BIOCHEMICALS: alpha- **crystallin** --structure, chaperone-like activity; **arginine hydrochloride** ; alpha-A **crystallin** ; alpha-B **crystallin** ; aminoguanidine hydrochloride

METHODS & EQUIPMENT: far-UV circular dichroism spectroscopy--laboratory techniques, spectrum analysis techniques; near-UV circular dichroism spectroscopy--laboratory techniques, spectrum analysis techniques; fluorescence assay--laboratory techniques, spectrum analysis techniques; glycerol gradient sedimentation--laboratory techniques

MISCELLANEOUS TERMS: drug development

CONCEPT CODES:

10060 Biochemistry studies - General

17506 Muscle - Pathology

20004 Sense organs - Physiology and biochemistry

BIOSYSTEMATIC CODES:
85715 Bovidae
86215 Hominidae

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CHEMICALS & BIOCHEMICALS: alpha- **crystallin** --...

... **arginine hydrochloride** ; ...

...alpha-A **crystallin** ; ...

...alpha-B **crystallin** ;

7/9,K/3 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

14246175 Genuine Article#: 953HG Number of References: 44
Title: Modulation of alpha- crystallin **chaperone activity in diabetic rat**

lens by curcumin

Author(s): Kumar PA; Suryanarayana P; Reddy PY; Reddy GB (REPRINT)
Corporate Source: Natl Inst Nutr,Hyderabad 500007/Andhra Pradesh/India/ (REPRINT); Natl Inst Nutr,Hyderabad 500007/Andhra Pradesh/India/(geereddy@yahoo.com)
Journal: MOLECULAR VISION, 2005, V11, N66 (JUL 26), P561-568
ISSN: 1090-0535 Publication date: 20050726
Publisher: MOLECULAR VISION, C/O JEFF BOATRIGHT, LAB B, 5500 EMORY EYE CENTER, 1327 CLIFTON RD, N E, ATLANTA, GA 30322 USA
Language: English Document Type: ARTICLE
Geographic Location: India
Journal Subject Category: BIOCHEMISTRY & MOLECULAR BIOLOGY; OPHTHALMOLOGY
Abstract: Purpose: A decline in the chaperone-like activity of eye lens alpha- **crystallin** in diabetic conditions has been reported. In this study, we investigated whether curcumin, a dietary antioxidant, can manipulate the chaperone-like activity of alpha- **crystallin** in diabetic rat lens.

Methods: A group of rats received ip injection of streptozotocin (STZ; 35 mg/kg body weight in buffer) to induce hyperglycemia, while another group of rats received only buffer as vehicle and served as control. STZ-treated rats were assigned to 3 groups and fed either no curcumin or 0.002% or 0.01% curcumin, respectively. Cataract progression due to hyperglycemia was monitored with a slit lamp biomicroscope. At the end of 8 weeks animals were sacrificed and lenses were collected. alpha H- and alpha L-crystallins from a set of pooled lenses in each group were isolated by gel filtration. Chaperone activity, hydrophobicity, and secondary and tertiary structure of alpha H- and alpha L-crystallins were assessed by light scattering/spectroscopic methods.

Results: A decrease in chaperone-like activity of alpha H- and alpha L-crystallins was observed in STZ-treated diabetic rats. The declined chaperone-like activity due to hyperglycemia was associated with reduced hydrophobicity and altered secondary and tertiary structure of alpha H- and alpha L-crystallins. Interestingly, alpha H- and alpha L-crystallins isolated from curcumin fed diabetic rat lenses had shown improved chaperone-like activity as compared to alpha H- and alpha L-crystallins from untreated diabetic rat lens. Feeding of curcumin prevented the alterations in hydrophobicity and structural changes due to STZ-induced hyperglycemia. Modulation of functional and structural properties by curcumin was found to be greater with the alpha L- **crystallin** than alpha H- **crystallin** . Loss of chaperone activity of alpha- **crystallin** , particularly alpha L- **crystallin** , in diabetic rat lens could be attributed at least partly to increased oxidative stress. Being an antioxidant, curcumin feeding has prevented the loss of alpha- **crystallin** chaperone activity and delayed the progression and maturation of diabetic cataract.

Conclusions: We demonstrate that curcumin, at the levels close to dietary consumption, prevented the loss of chaperone-like activity of alpha- **crystallin** vis-a-vis cataractogenesis due to diabetes in rat lens.
Identifiers--KeyWord Plus(R): A- **CRYSTALLIN** ; B- **CRYSTALLIN** ; **ARGININE HYDROCHLORIDE** ; IN-VIVO; CATARACT; AGGREGATION; PROTECT; STRESS; INDIA; RISK

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YANG FS, 2005, V280, P5892, J BIOL CHEM

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Methods: A group of rats received ip injection of streptozotocin (STZ...

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7/9,K/4 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

13835968 Genuine Article#: 915KO Number of References: 49
Title: Arginine hydrochloride **enhances the dynamics of subunit assembly and the chaperone-like activity of alpha-** crystallin
Author(s): Srinivas V; Raman B; Rao KS; Ramakrishna T; Rao CM (REPRINT)
Corporate Source: Ctr Cellular & Mol Biol,Uppal Rd/Hyderabad 500007/Andhra Pradesh/India/ (REPRINT); Ctr Cellular & Mol Biol,Hyderabad 500007/Andhra Pradesh/India/(mohan@ccmb.res.in)
Journal: MOLECULAR VISION, 2005, V11, N27-29 (APR 1), P249-255
ISSN: 1090-0535 Publication date: 20050401
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Abstract: Purpose: alpha- **Crystallin** , a major eye lens protein, bears homology with small heat shock proteins (sHsps) and exhibits molecular chaperone-like activity. Structural perturbation by temperature or low concentrations of denaturants leads to enhancement of its chaperone-like activity. We have earlier demonstrated similar enhancement of chaperone-like activity using biologically compatible solutes such as **arginine hydrochloride** and aminoguanidine. The purpose of the present study is to get an insight into the mechanism of the arginine induced enhancement of chaperone-like activity of alpha- **crystallin** .

Methods: The effect of **arginine hydrochloride** on the chaperone-like activity of alpha- **crystallin** at 25 degrees C was studied using DTT induced aggregation of insulin as a model system. Changes in the accessibility of the thiol group near the end of the alpha- **crystallin** domain in the absence and the presence of **arginine hydrochloride** were studied using dithiobisnitrobenzoic acid. Fluorescence resonance energy transfer studies were performed to investigate changes in the dynamics of the subunit assembly. Urea induced denaturation studies of alpha- **crystallin** were carried out to investigate structural destabilization of alpha- **crystallin** , if any, in the presence of **arginine hydrochloride** .

Results: **Arginine hydrochloride** increases the chaperone-like activity of alpha- **crystallin** several fold towards DTT induced aggregation of insulin at room temperature. Our study shows that both the extent and the rate of accessibility of the thiol group are increased in the presence of arginine. Fluorescence resonance energy transfer experiments show that **arginine hydrochloride** significantly increases the subunit exchange between the oligomers of alpha- **crystallin** . Arginine induced structural perturbation and loosening of subunit assembly of alpha- **crystallin** leads to overall destabilization of the protein as reflected by the urea denaturation study.

Conclusions: Arginine perturbs the tertiary and quaternary structure of alpha- **crystallin** and enhances the dynamics of the subunit assembly leading to enhanced chaperone-like activity. Thus, in addition to size, surface hydrophobicity, and charge distribution, the dynamics of the subunit assembly appears to be one of the critical factors that can modulate the chaperone activity.

Identifiers--KeyWord Plus(R): HEAT-SHOCK-PROTEIN; DESMIN-RELATED MYOPATHY; QUATERNARY STRUCTURE; MOLECULAR CHAPERONE; A- **CRYSTALLIN** ; B- **CRYSTALLIN** ; STRUCTURAL PERTURBATION; HYDROPHOBIC SURFACES; MISSENSE MUTATION; ENERGY-TRANSFER

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Conclusions: Arginine perturbs the tertiary and quaternary structure of alpha- **crystallin** and enhances the dynamics of the subunit assembly leading to enhanced chaperone-like activity. Thus...

...Identifiers--HEAT-SHOCK-PROTEIN; DESMIN-RELATED MYOPATHY; QUATERNARY STRUCTURE; MOLECULAR CHAPERONE; A- **CRYSTALLIN** ; B- **CRYSTALLIN** ; STRUCTURAL PERTURBATION; HYDROPHOBIC SURFACES; MISSENSE MUTATION; ENERGY-TRANSFER

7/9,K/5 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

11679571 Genuine Article#: 681LC Number of References: 57
Title: Structural perturbation and enhancement of the chaperone-like activity of alpha- crystallin **by** arginine hydrochloride
Author(s): Srinivas V; Raman B; Rao KS; Ramakrishna T; Rao CM (REPRINT)
Corporate Source: Ctr Cellular & Mol Biol,Uppal Rd/Hyderabad 500007/Andhra Pradesh/India/ (REPRINT); Ctr Cellular & Mol Biol,Hyderabad 500007/Andhra Pradesh/India/
Journal: PROTEIN SCIENCE, 2003, V12, N6 (JUN), P1262-1270
ISSN: 0961-8368 Publication date: 20030600
Publisher: COLD SPRING HARBOR LAB PRESS, PUBLICATIONS DEPT, 500 SUNNYSIDE BLVD, WOODBURY, NY 11797-2924 USA
Language: English Document Type: ARTICLE
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Journal Subject Category: BIOCHEMISTRY & MOLECULAR BIOLOGY
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Descriptors--Author Keywords: chaperone-like activity ; alpha- **crystallin** ; arginine ; aminoguanidine ; structural perturbation
Identifiers--KeyWord Plus(R): HEAT-SHOCK-PROTEIN; DESMIN-RELATED MYOPATHY; B- **CRYSTALLIN** ; MOLECULAR CHAPERONE; A- **CRYSTALLIN** ; IN-VITRO; HYDROPHOBIC SURFACES; MISSENSE MUTATION; THERMAL-STRESS; LENS
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Title: Structural perturbation and enhancement of the chaperone-like activity of alpha- crystallin **by** arginine hydrochloride

Abstract: Structural perturbation of a- **crystallin** is shown to enhance its

molecular chaperone-like activity in preventing aggregation of target proteins...

...and negatively charged side-chains, increases the chaperone-like activity of calf eye lens alpha- **crystallin** as well as recombinant human alphaA- and alphaB-crystallins. Arginine-induced increase in the chaperone activity is more pronounced for alphaB- **crystallin** than for alphaA- **crystallin** . Other guanidinium compounds such as aminoguanidine hydrochloride and guanidine hydrochloride also show a similar effect, but to different extents. A point mutation, R120G, in alphaB- **crystallin** that is associated with desmin-related myopathy, results in a significant loss of chaperone-like...

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...Identifiers--HEAT-SHOCK-PROTEIN; DESMIN-RELATED MYOPATHY; B- **CRYSTALLIN** ; MOLECULAR CHAPERONE; A- **CRYSTALLIN** ; IN-VITRO; HYDROPHOBIC SURFACES; MISSENSE MUTATION; THERMAL-STRESS; LENS

7/9,K/6 (Item 1 from file: 71)

02344455 2003128140

Structural perturbation and enhancement of the chaperone-like activity of alpha- crystallin by arginine hydrochloride

Srinivas V.; Raman B.; Rao K.S.; Ramakrishna T.; Rao Ch.M.
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PUBLICATION DATE: June 1, 2003
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ISSN: 0961-8368
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 57

Structural perturbation of alpha- **crystallin** is shown to enhance its molecular chaperone-like activity in preventing aggregation of target proteins. We demonstrate that arginine, a biologically compatible molecule that is known to bind to the peptide backbone and negatively charged side-chains, increases the chaperone-like activity of calf eye lens alpha-

crystallin as well as recombinant human alphaA- and alphaB-crystallins. Arginineinduced increase in the chaperone activity is more pronounced for alphaB- **crystallin** than for alphaA- **crystallin** . Other guanidinium compounds such as aminoguanidine hydrochloride and guanidine hydrochloride also show a similar effect, but to different extents. A point mutation, R120G, in alphaB- **crystallin** that is associated with desmin-related myopathy, results in a significant loss of chaperone-like activity. Arginine restores the activity of mutant protein to a considerable extent. We have investigated the effect of arginine on the structural changes of alpha- **crystallin** by circular dichroism, fluorescence, and glycerol gradient sedimentation. Far-UV CD spectra show no significant changes in secondary structure, whereas near-UV CD spectra show subtle changes in the presence of arginine. Glycerol gradient sedimentation shows a significant decrease in the size of alpha- **crystallin** oligomer in the presence of arginine. Increased exposure of hydrophobic surfaces of alpha- **crystallin** , as monitored by pyrene-solubilization and ANS-fluorescence, is observed in the presence of arginine. These results show that arginine brings about subtle changes in the tertiary structure and significant changes in the quaternary structure of alpha- **crystallin** and enhances its chaperone-like activity significantly. This study should prove useful in designing strategies to improve chaperone function for therapeutic applications.

DESCRIPTORS:
Chaperone-like activity; alpha- **crystallin** ; Arginine; Aminoguanidine; Structural perturbation

CLASSIFICATION CODE AND DESCRIPTION:
82.2.8 - PROTEIN BIOCHEMISTRY / STRUCTURAL STUDIES / Folding, Unfolding and Stability

Structural perturbation and enhancement of the chaperone-like activity of alpha- crystallin **by** arginine hydrochloride

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...subtle changes in the tertiary structure and significant changes in the quaternary structure of alpha- **crystallin** and enhances its chaperone-like activity significantly. This study should prove useful in designing strategies...

DESCRIPTORS:
Chaperone-like activity; alpha- **crystallin** ; Arginine; Aminoguanidine; Structural perturbation

7/9,K/7 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

13357267 EMBASE No: 2005431360
Arginine hydrochloride **enhances the dynamics of subunit assembly and the chaperone-like activity of alpha-** crystallin
Srinivas V.; Raman B.; Sridhar Rao K.; Ramakrishna T.; Mohan Rao Ch.
Dr. Ch. Mohan Rao, Centre for Cellular and Molecular Biology, Uppal Road, Hyderabad 500 007 India
AUTHOR EMAIL: mohan@ccmb.res.in
Molecular Vision (MOL. VISION) (United States) 01 APR 2005, 11/- (249-255)
CODEN: MVEPF ISSN: 1090-0535
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 49

Purpose: alpha- **Crystallin** , a major eye lens protein, bears homology with small heat shock proteins (sHsps) and exhibits molecular chaperone-like activity. Structural perturbation by temperature or low concentrations of denaturants leads to enhancement of its chaperone-like activity. We have earlier demonstrated similar enhancement of chaperone-like activity using biologically compatible solutes such as **arginine hydrochloride** and aminoguanidine. The purpose of the present study is to get an insight into the mechanism of the arginine induced enhancement of chaperone-like activity of **crystallin** . Methods: The effect of **arginine hydrochloride** on the chaperone-like activity of alpha-**crystallin** at 25 degreesC was studied using DTT induced aggregation of insulin as a model system. Changes in the accessibility of the thiol group near the end of the a- **crystallin** domain in the absence and the presence of **arginine hydrochloride** were studied using dithiobisnitrobenzoic acid. Fluorescence resonance energy transfer studies were performed to investigate changes in the dynamics of the subunit assembly. Urea induced denaturation studies of alpha- **crystallin** were carried out to investigate structural destabilization of alpha- **crystallin** , if any, in the presence of **arginine hydrochloride** . Results: **Arginine hydrochloride** increases the chaperone-like activity of alpha- **crystallin** several fold towards DTT induced aggregation of insulin at room temperature. Our study shows that both the extent and the rate of accessibility of the thiol group are increased in the presence of arginine. Fluorescence resonance energy transfer experiments show that **arginine hydrochloride** significantly increases the subunit exchange between the oligomers of alpha- **crystallin** . Arginine induced structural perturbation and loosening of subunit assembly of alpha- **crystallin** leads to overall destabilization of the protein as reflected by the urea denaturation study. Conclusions: Arginine perturbs

the tertiary and quaternary structure of a- **crystallin** and enhances the dynamics of the subunit assembly leading to enhanced chaperone-like activity. Thus, in addition to size, surface hydrophobicity, and charge distribution, the dynamics of the subunit assembly appears to be one of the critical factors that can modulate the chaperone activity. (c)2005 Molecular Vision.

DRUG DESCRIPTORS:
*arginine; *chaperone; *alpha **crystallin**
dithiothreitol; insulin; benzoic acid; urea
MEDICAL DESCRIPTORS:
protein assembly; biological model; protein domain; fluorescence resonance energy transfer; protein denaturation; protein structure; room temperature; hydrophobicity; article; priority journal
CAS REGISTRY NO.: 1119-34-2, 15595-35-4, 7004-12-8, 74-79-3 (arginine); 3483-12-3 (dithiothreitol); 9004-10-8 (insulin); 532-32-1, 582-25-2, 65-85-0, 766-76-7 (benzoic acid); 57-13-6 (urea)
SECTION HEADINGS:
029 Clinical and Experimental Biochemistry

Arginine hydrochloride **enhances the dynamics of subunit assembly and the chaperone-like activity of alpha-** crystallin
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DRUG DESCRIPTORS:
*arginine; *chaperone; *alpha **crystallin**

7/9,K/8 (Item 2 from file: 73)

12095641 EMBASE No: 2003207170

Structural perturbation and enhancement of the chaperone-like activity of alpha- crystallin by arginine hydrochloride

Srinivas V.; Raman B.; Rao K.S.; Ramakrishna T.; Rao Ch.M.
Ch.M. Rao, Ctr. for Cell. and Molecular Biology, Uppal Road, Hyderabad 500 007 India
AUTHOR EMAIL: mohan@ccmb.res.in

Protein Science (PROTEIN SCI.) (United States) 01 JUN 2003, 12/6 (1262-1270)
CODEN: PRCIE ISSN: 0961-8368
DOCUMENT TYPE: Journal ; Article
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DRUG DESCRIPTORS:
*chaperone; *alpha **crystallin** --endogenous compound--ec; *arginine
guanidine derivative; aminoguanidine; guanidine hydrochloride; desmin; glycerol; pyrene; oligomer; unclassified drug
MEDICAL DESCRIPTORS:
*protein structure
structure analysis; protein targeting; protein binding; point mutation; circular dichroism; fluorescence; sedimentation; protein secondary structure; solubilization; protein tertiary structure; protein quaternary structure; nonhuman; article; priority journal
DRUG TERMS (UNCONTROLLED): alpha b **crystallin**
CAS REGISTRY NO.: 1119-34-2, 15595-35-4, 7004-12-8, 74-79-3 (arginine); 1068-42-4, 2582-30-1, 79-17-4 (aminoguanidine); 50-01-1 (guanidine

hydrochloride); 56-81-5 (glycerol); 129-00-0 (pyrene)
SECTION HEADINGS:
029 Clinical and Experimental Biochemistry

Structural perturbation and enhancement of the chaperone-like activity of alpha- crystallin **by** arginine hydrochloride

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DRUG DESCRIPTORS:
*chaperone; *alpha **crystallin** --endogenous compound--ec; *arginine
DRUG TERMS (UNCONTROLLED): alpha b **crystallin**

7/9,K/9 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

20362892 PMID: 15827547
Arginine hydrochloride **enhances the dynamics of subunit assembly and the chaperone-like activity of alpha-** crystallin .
Srinivas V; Raman B; Rao K Sridhar; Ramakrishna T; Rao Ch Mohan
Centre for Cellular and Molecular Biology, Hyderabad, India.
Molecular vision electronic resource (United States) 2005, 11 p249-55, ISSN 1090-0535--Electronic Journal Code: 9605351
Publishing Model Electronic
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS

PURPOSE: Alpha- **crystallin** , a major eye lens protein, bears homology with small heat shock proteins (sHsps) and exhibits molecular chaperone-like activity. Structural perturbation by temperature or low concentrations of denaturants leads to enhancement of its chaperone-like activity. We have earlier demonstrated similar enhancement of chaperone-like activity using biologically compatible solutes such as **arginine hydrochloride** and aminoguanidine. The purpose of the present study is to get an insight into the mechanism of the arginine induced enhancement of chaperone-like activity of alpha- **crystallin** . METHODS: The effect of **arginine hydrochloride** on the chaperone-like activity of alpha- **crystallin** at 25 degrees C was studied using DTT induced aggregation of insulin as a model system. Changes in the accessibility of the thiol group near the end of the alpha- **crystallin** domain in the absence and the presence of **arginine hydrochloride** were studied using dithiobisnitrobenzoic acid. Fluorescence resonance energy transfer studies were performed to investigate changes in the dynamics of the subunit assembly. Urea induced denaturation studies of alpha- **crystallin** were carried out to investigate structural destabilization of alpha- **crystallin** , if any, in the presence of **arginine hydrochloride** . RESULTS: **Arginine hydrochloride** increases the chaperone-like activity of alpha- **crystallin** several fold towards DTT induced aggregation of insulin at room temperature. Our study shows that both the extent and the rate of accessibility of the thiol group are increased in the presence of arginine. Fluorescence resonance energy transfer experiments show that **arginine hydrochloride** significantly increases the subunit exchange between the oligomers of alpha- **crystallin** . Arginine induced structural perturbation and loosening of subunit assembly of alpha- **crystallin** leads to overall destabilization of the protein as reflected by the urea denaturation study. CONCLUSIONS: Arginine perturbs the tertiary and quaternary structure of alpha- **crystallin** and enhances the dynamics of the subunit assembly leading to enhanced chaperone-like activity. Thus, in addition to size, surface hydrophobicity, and charge distribution, the dynamics of the subunit assembly appears to be one of the critical factors that can modulate the chaperone activity.

Descriptors: *Arginine--pharmacology--PD; *Molecular Chaperones --metabolism--ME; *alpha-Crystallins--drug effects--DE; Animals; Cattle; Disulfides; Dithiothreitol; Fluorescent Dyes; Lens, Crystalline--chemistry --CH; Protein Subunits--chemistry--CH; Protein Subunits--metabolism--ME; Recombinant Proteins--chemistry--CH; Recombinant Proteins--drug effects --DE; Recombinant Proteins--metabolism--ME; Solubility; Spectrometry, Fluorescence; alpha-Crystallins--chemistry--CH; alpha-Crystallins --metabolism--ME

CAS Registry No.: 0 (Disulfides); 0 (Fluorescent Dyes); 0 (Molecular Chaperones); 0 (Protein Subunits); 0 (Recombinant Proteins); 0 (alpha-Crystallins); 3483-12-3 (Dithiothreitol); 74-79-3 (Arginine)

Record Date Created: 20050413

Record Date Completed: 20060413

Date of Electronic Publication: 20050401

Arginine hydrochloride **enhances the dynamics of subunit assembly and the chaperone-like activity of alpha-** crystallin .

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7/9,K/10 (Item 2 from file: 155)

14316050 PMID: 12761397

Structural perturbation and enhancement of the chaperone-like activity of alpha- crystallin **by** arginine hydrochloride **.**

Srinivas Volety; Raman Bakthisaran; Rao Kunchala Sridhar; Ramakrishna Tangirala; Rao Ch Mohan

Centre for Cellular & Molecular Biology, Hyderabad 500 007, India.

Protein science - a publication of the Protein Society (United States) Jun 2003, 12 (6) p1262-70, ISSN 0961-8368--Print Journal Code: 9211750

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Languages: ENGLISH
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Subfile: INDEX MEDICUS

Structural perturbation of alpha- **crystallin** is shown to enhance its molecular chaperone-like activity in preventing aggregation of target proteins. We demonstrate that arginine, a biologically compatible molecule that is known to bind to the peptide backbone and negatively charged side-chains, increases the chaperone-like activity of calf eye lens alpha- **crystallin** as well as recombinant human alphaA- and alphaB-crystallins. Arginine-induced increase in the chaperone activity is more pronounced for alphaB- **crystallin** than for alphaA- **crystallin** . Other guanidinium compounds such as aminoguanidine hydrochloride and guanidine hydrochloride also show a similar effect, but to different extents. A point mutation, R120G, in alphaB- **crystallin** that is associated with desmin-related myopathy, results in a significant loss of chaperone-like activity.

Arginine restores the activity of mutant protein to a considerable extent. We have investigated the effect of arginine on the structural changes of alpha- **crystallin** by circular dichroism, fluorescence, and glycerol gradient sedimentation. Far-UV CD spectra show no significant changes in secondary structure, whereas near-UV CD spectra show subtle changes in the presence of arginine. Glycerol gradient sedimentation shows a significant decrease in the size of alpha- **crystallin** oligomer in the presence of arginine. Increased exposure of hydrophobic surfaces of alpha- **crystallin** , as monitored by pyrene-solubilization and ANS-fluorescence, is observed in the presence of arginine. These results show that arginine brings about subtle changes in the tertiary structure and significant changes in the quaternary structure of alpha- **crystallin** and enhances its chaperone-like activity significantly. This study should prove useful in designing strategies to improve chaperone function for therapeutic applications.

Descriptors: *Arginine--pharmacology--PD; *Crystallins--chemistry--CH; Animals; Cattle; Centrifugation, Density Gradient; Circular Dichroism; Crystallins--metabolism--ME; Dithiothreitol; Guanidine--pharmacology--PD; Insulin--chemistry--CH; Insulin--metabolism--ME; Protein Conformation --drug effects--DE; Pyrenes--chemistry--CH; Solubility; Spectrometry, Fluorescence; Time Factors

CAS Registry No.: 0 (Crystallins); 0 (Pyrenes); 11061-68-0 (Insulin) ; 113-00-8 (Guanidine); 129-00-0 (pyrene); 3483-12-3 (Dithiothreitol) ; 74-79-3 (Arginine)

Record Date Created: 20030522

Record Date Completed: 20041005

Structural perturbation and enhancement of the chaperone-like activity of alpha- crystallin **by** arginine hydrochloride **.**

Structural perturbation of alpha- **crystallin** is shown to enhance its molecular chaperone-like activity in preventing aggregation of target proteins...

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```
? s arginine and hydrochloride
          416125  ARGININE
          382785  HYDROCHLORIDE
      S8    4708  ARGININE AND HYDROCHLORIDE
? s s1 and s8
           40380  S1
            4708  S8
      S9      20  S1 AND S8
? t s9/9,k/1-5

 9/9,K/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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0016021600   BIOSIS NO.: 200600366995
Effect of site-directed mutagenesis of methylglyoxal-modifiable arginine
  residues on the structure and chaperone function of human alpha A-
  crystallin
AUTHOR: Biswas Ashis; Miller Antonia; Oya-Ito Tomoko; Santhoshkumar Puttur;
  Bhat Manjunatha; Nagaraj Ram H (Reprint)
AUTHOR ADDRESS: Case Western Reserve Univ, Dept Ophthalmol, Cleveland, OH
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AUTHOR E-MAIL ADDRESS: ram.nagaraj@case.edu
JOURNAL: Biochemistry  45 (14): p4569-4577 APR 11 2006 2006
ISSN: 0006-2960
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We reported previously that chemical modification of human alpha
  A- crystallin by a metabolic dicarbonyl compound, methylglyoxal (MGO),
  enhances its chaperone-like function, a phenomenon which we attributed to
  formation of argpyrimidine at arginine residues (R) 21 49, and 103.
  This structural change removes the positive charge on the arginine
  residues. To explore this mechanism further, we replaced these three R
  residues with a neutral alanine (A) residue one at a time or in
  combination and examined the impact on the structure and chaperone
  function. Measurement of intrinsic tryptophan fluorescence and near-UV CD
  spectra revealed alteration of the microenvironment of aromatic amino
  acid residues in mutant proteins. When compared to wild-type (wt) alpha
  A- crystallin , the chaperone function of R21A and R103A mutants
  increased 20% and 18% as measured by the insulin aggregation assay and
  increased it as much as 39% and 28% when measured by the citrate synthase
  (CS) aggregation assay. While the R49A mutant lost most of its chaperone
  function, R21A/R103A and R21A/R49A/R103A mutants had slightly better
  function (6-14% and 10-14%) than the wt protein in these assays. R21A and
  R103A mutants had higher surface hydrophobicity than wt alpha A-
  crystallin , but the R49A mutant had lower hydrophobicity. R21A and R103A
  mutants, but not the R49A mutant, were more efficient than wt protein in
  refolding guanidine hydrochloride -treated malate dehydrogenase to its
  native state. Our findings indicate that the positive charges on R21,
  R49, and R103 are important determinants of the chaperone function of
  alpha A- crystallin and suggest that chemical modification of arginine
  residues may play a role in protein aggregation during lens aging and
  cataract formation.

REGISTRY NUMBERS: 78-98-8: methylglyoxal
```

DESCRIPTORS:
MAJOR CONCEPTS: Biochemistry and Molecular Biophysics
BIOSYSTEMATIC NAMES: Enterobacteriaceae--Facultatively Anaerobic Gram-Negative Rods, Eubacteria, Bacteria, Microorganisms
ORGANISMS: Escherichia coli (Enterobacteriaceae)--expression system
COMMON TAXONOMIC TERMS: Bacteria; Eubacteria; Microorganisms
CHEMICALS & BIOCHEMICALS: methylglyoxal {MGO}; alpha-A- **crystallin** -- methylglyoxal-modifiable **arginine** residue
METHODS & EQUIPMENT: site-directed mutagenesis--laboratory techniques, genetic techniques
CONCEPT CODES:
10060 Biochemistry studies - General
31000 Physiology and biochemistry of bacteria
BIOSYSTEMATIC CODES:
06702 Enterobacteriaceae

Effect of site-directed mutagenesis of methylglyoxal-modifiable arginine **residues on the structure and chaperone function of human alpha A-** crystallin

ABSTRACT: We reported previously that chemical modification of human alpha A- **crystallin** by a metabolic dicarbonyl compound, methylglyoxal (MGO), enhances its chaperone-like function, a phenomenon which we attributed to formation of argpyrimidine at **arginine** residues (R) 21 49, and 103. This structural change removes the positive charge on the **arginine** residues. To explore this mechanism further, we replaced these three R residues with a neutral...

...aromatic amino acid residues in mutant proteins. When compared to wild-type (wt) alpha A- **crystallin** , the chaperone function of R21A and R103A mutants increased 20% and 18% as measured by...

...in these assays. R21A and R103A mutants had higher surface hydrophobicity than wt alpha A- **crystallin** , but the R49A mutant had lower hydrophobicity. R21A and R103A mutants, but not the R49A mutant, were more efficient than wt protein in refolding guanidine **hydrochloride** -treated malate dehydrogenase to its native state. Our findings indicate that the positive charges on R21, R49, and R103 are important determinants of the chaperone function of alpha A- **crystallin** and suggest that chemical modification of **arginine** residues may play a role in protein aggregation during lens aging and cataract formation.
DESCRIPTORS:
CHEMICALS & BIOCHEMICALS: ...alpha-A- **crystallin** --...
...methylglyoxal-modifiable **arginine** residue

9/9,K/2 (Item 2 from file: 5)

0015321550 BIOSIS NO.: 200510016050
Arginine hydrochloride **enhances the dynamics of subunit assembly and the chaperone-like activity of alpha-** crystallin
AUTHOR: Srinivas V; Raman B; Rao K Sridhar; Ramakrishna T; Rao Ch Mohan (Reprint)
AUTHOR ADDRESS: Ctr Cellular and Mol Biol, Uppal Rd, Hyderabad 500007, Andhra Pradesh, India**India

AUTHOR E-MAIL ADDRESS: mohan@ccmb.res.in
JOURNAL: Molecular Vision 11 (27-29): p249-255 APR 1 05 2005
ISSN: 1090-0535
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Purpose: alpha- **Crystallin** , a major eye lens protein, bears homology with small heat shock proteins (sHsps) and exhibits molecular chaperone-like activity. Structural perturbation by temperature or low concentrations of denaturants leads to enhancement of its chaperone-like activity. We have earlier demonstrated similar enhancement of chaperone-like activity using biologically compatible solutes such as **arginine hydrochloride** and aminoguanidine. The purpose of the present study is to get an insight into the mechanism of the **arginine** induced enhancement of chaperone-like activity of alpha- **crystallin** .Methods: The effect of **arginine hydrochloride** on the chaperone-like activity of alpha- **crystallin** at 25 degrees C was studied using DTT induced aggregation of insulin as a model system. Changes in the accessibility of the thiol group near the end of the alpha- **crystallin** domain in the absence and the presence of **arginine hydro**chloride were studied using dithiobisnitrobenzoic acid. Fluorescence resonance energy transfer studies were performed to investigate changes in the dynamics of the subunit assembly. Urea induced denaturation studies of alpha- **crystallin** were carried out to investigate structural destabilization of alpha- **crystallin** , if any, in the presence of **arginine hydrochloride** .Results: **Arginine hydrochloride** increases the chaperone-like activity of alpha- **crystallin** several fold towards DTT induced aggregation of insulin at room temperature. Our study shows that both the extent and the rate of accessibility of the thiol group are increased in the presence of **arginine** . Fluorescence resonance energy transfer experiments show that **arginine hydrochloride** significantly increases the subunit exchange between the oligomers of alpha- **crystallin** . **Arginine** induced structural perturbation and loosening of subunit assembly of alpha- **crystallin** leads to overall destabilization of the protein as reflected by the urea denaturation study.Conclusions: **Arginine** perturbs the tertiary and quaternary structure of alpha- **crystallin** and enhances the dynamics of the subunit assembly leading to enhanced chaperone-like activity. Thus, in addition to size, surface hydrophobicity, and charge distribution, the dynamics of the subunit assembly appears to be one of the critical factors that can modulate the chaperone activity.

REGISTRY NUMBERS: 9004-10-8: insulin; 79-17-4: aminoguanidine; 32042-43-6: **arginine hydrochloride**
DESCRIPTORS:
MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Sense Organs--Sensory Reception
ORGANISMS: PARTS ETC: eye lens
CHEMICALS & BIOCHEMICALS: insulin; small heat shock proteins; aminoguanidine; **arginine hydrochloride** ; alpha- **crystallin** -- chaperone-like activity
CONCEPT CODES:
10060 Biochemistry studies - General
10064 Biochemistry studies - Proteins, peptides and amino acids
20004 Sense organs - Physiology and biochemistry

Arginine hydrochloride **enhances the dynamics of subunit assembly and the chaperone-like activity of alpha-** crystallin

ABSTRACT: Purpose: alpha- **Crystallin** , a major eye lens protein, bears homology with small heat shock proteins (sHsps) and exhibits...

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...REGISTRY NUMBERS: **arginine hydrochloride**

DESCRIPTORS:

CHEMICALS & BIOCHEMICALS: ... **arginine hydrochloride** ; ...

...alpha- **crystallin** --

9/9,K/3 (Item 3 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

0014361712 BIOSIS NO.: 200300320431

Structural perturbation and enhancement of the chaperone-like activity of alpha- crystallin **by** arginine hydrochloride .

AUTHOR: Srinivas Volety; Raman Bakthisaran; Rao Kunchala Sridhar; Ramakrishna Tangirala; Rao Ch Mohan (Reprint)

AUTHOR ADDRESS: Centre for Cellular and Molecular Biology, Uppal Road, Hyderabad, 500 007, India**India

AUTHOR E-MAIL ADDRESS: mohan@ccmb.res.in

JOURNAL: Protein Science 12 (6): p1262-1270 June 2003 2003

MEDIUM: print

ISSN: 0961-8368

DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Structural perturbation of alpha- **crystallin** is shown to enhance its molecular chaperone-like activity in preventing aggregation of target proteins. We demonstrate that **arginine** , a biologically compatible molecule that is known to bind to the peptide backbone and negatively charged side-chains, increases the chaperone-like activity of calf eye lens alpha- **crystallin** as well as recombinant human alphaA- and alphaB-crystallins. **Arginine** -induced increase in the chaperone activity is more pronounced for alphaB- **crystallin** than for alphaA- **crystallin** . Other guanidinium compounds such as aminoguanidine **hydrochloride** and guanidine **hydrochloride** also show a similar effect, but to different extents. A point mutation, R120G, in alphaB- **crystallin** that is associated with desmin-related myopathy, results in a significant loss of chaperone-like activity. **Arginine** restores the activity of mutant protein to a considerable extent. We have investigated the effect of **arginine** on the structural changes of alpha- **crystallin** by circular dichroism, fluorescence, and glycerol gradient sedimentation. Far-UV CD spectra show no significant changes in secondary structure, whereas near-UV CD spectra show subtle changes in the presence of **arginine** . Glycerol gradient sedimentation shows a significant decrease in the size of alpha- **crystallin** oligomer in the presence of **arginine** . Increased exposure of hydrophobic surfaces of alpha- **crystallin** , as monitored by pyrene-solubilization and ANS-fluorescence, is observed in the presence of **arginine** . These results show that **arginine** brings about subtle changes in the tertiary structure and significant changes in the quaternary structure of alpha- **crystallin** and enhances its chaperone-like activity significantly. This study should prove useful in designing strategies to improve chaperone function for therapeutic applications.

REGISTRY NUMBERS: 1119-34-2Q: **arginine** **hydrochloride** ; 15595-35-4Q: **arginine** **hydrochloride** ; 32042-43-6Q: **arginine** **hydrochloride** ; 1937-19-5Q: aminoguanidine **hydrochloride** ; 16139-18-7Q: aminoguanidine **hydrochloride**

DESCRIPTORS:

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics

BIOSYSTEMATIC NAMES: Bovidae--Artiodactyla, Mammalia, Vertebrata, Chordata, Animalia; Hominidae--Primates, Mammalia, Vertebrata, Chordata , Animalia

ORGANISMS: cow (Bovidae); human (Hominidae)

ORGANISMS: PARTS ETC: lens--sensory system

COMMON TAXONOMIC TERMS: Artiodactyls; Nonhuman Vertebrates; Nonhuman Mammals; Animals; Chordates; Humans; Mammals; Primates; Vertebrates

DISEASES: desmin-related myopathy--muscle disease

CHEMICALS & BIOCHEMICALS: alpha- **crystallin** --structure, chaperone-like activity; **arginine** **hydrochloride** ; alpha-A **crystallin** ; alpha-B **crystallin** ; aminoguanidine **hydrochloride**

METHODS & EQUIPMENT: far-UV circular dichroism spectroscopy--laboratory techniques, spectrum analysis techniques; near-UV circular dichroism spectroscopy--laboratory techniques, spectrum analysis techniques; fluorescence assay--laboratory techniques, spectrum analysis techniques; glycerol gradient sedimentation--laboratory techniques

MISCELLANEOUS TERMS: drug development

CONCEPT CODES:

10060 Biochemistry studies - General
17506 Muscle - Pathology
20004 Sense organs - Physiology and biochemistry
BIOSYSTEMATIC CODES:
85715 Bovidae
86215 Hominidae

Structural perturbation and enhancement of the chaperone-like activity of alpha- crystallin **by** arginine hydrochloride .

ABSTRACT: Structural perturbation of alpha- **crystallin** is shown to enhance its molecular chaperone-like activity in preventing aggregation of target proteins. We demonstrate that **arginine** , a biologically compatible molecule that is known to bind to the peptide backbone and negatively charged side-chains, increases the chaperone-like activity of calf eye lens alpha- **crystallin** as well as recombinant human alphaA- and alphaB-crystallins. **Arginine** -induced increase in the chaperone activity is more pronounced for alphaB- **crystallin** than for alphaA- **crystallin** . Other guanidinium compounds such as aminoguanidine **hydrochloride** and guanidine **hydrochloride** also show a similar effect, but to different extents. A point mutation, R120G, in alphaB- **crystallin** that is associated with desmin-related myopathy, results in a significant loss of chaperone-like activity. **Arginine** restores the activity of mutant protein to a considerable extent. We have investigated the effect of **arginine** on the structural changes of alpha- **crystallin** by circular dichroism, fluorescence, and glycerol gradient sedimentation. Far-UV CD spectra show no significant...

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...REGISTRY NUMBERS: **arginine hydrochloride** ; ...

... **arginine hydrochloride** ; ...

... **arginine hydrochloride** ; ...

...aminoguanidine **hydrochloride** ; ...

...aminoguanidine **hydrochloride**
DESCRIPTORS:
CHEMICALS & BIOCHEMICALS: alpha- **crystallin** --...

... **arginine hydrochloride** ; ...

...alpha-A **crystallin** ; ...

...alpha-B **crystallin** ; ...

...aminoguanidine **hydrochloride**

9/9,K/4 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

15023860 Genuine Article#: 031GH Number of References: 59
Title: Effect of site-directed mutagenesis of methylglyoxal-modifiable arginine **residues on the structure and chaperone function of human alpha A-** crystallin
Author(s): Biswas A; Miller A; Oya-Ito T; Santhoshkumar P; Bhat M; Nagaraj RH (REPRINT)
Corporate Source: Case Western Reserve Univ,Dept Ophthalmol,Cleveland//OH/44106 (REPRINT); Case Western Reserve Univ,Dept Ophthalmol,Cleveland//OH/44106; Case Western Reserve Univ,Dept Pharmacol,Cleveland//OH/44106; Cleveland Clin Fdn,Ctr Anesthesiol Res,Cleveland//OH/44195; Univ Missouri,Mason Eye Inst,Columbia//MO/65212(ram.nagaraj@case.edu)
Journal: BIOCHEMISTRY, 2006, V45, N14 (APR 11), P4569-4577
ISSN: 0006-2960 Publication date: 20060411
Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036 USA
Language: English Document Type: ARTICLE
Geographic Location: USA
Journal Subject Category: BIOCHEMISTRY & MOLECULAR BIOLOGY
Abstract: We reported previously that chemical modification of human alpha A- **crystallin** by a metabolic dicarbonyl compound, methylglyoxal (MGO), enhances its chaperone-like function, a phenomenon which we attributed to formation of argpyrimidine at **arginine** residues (R) 21 49, and 103. This structural change removes the positive charge on the **arginine** residues. To explore this mechanism further, we replaced these three R residues with a neutral alanine (A) residue one at a time or in combination and examined the impact on the structure and chaperone function. Measurement of intrinsic tryptophan fluorescence and near-UV CD spectra revealed alteration of the microenvironment of aromatic amino acid residues in mutant proteins. When compared to wild-type (wt) alpha A- **crystallin** , the chaperone function of R21A and R103A mutants increased 20% and 18% as measured by the insulin aggregation assay and increased it as much as 39% and 28% when measured by the citrate synthase (CS) aggregation assay. While the R49A mutant lost most of its chaperone function, R21A/R103A and R21A/R49A/R103A mutants had slightly better function (6-14% and 10-14%) than the wt protein in these assays. R21A and R103A mutants had higher surface hydrophobicity than wt alpha A- **crystallin** , but the R49A mutant had lower hydrophobicity. R21A and R103A mutants, but not the R49A mutant, were more efficient than wt protein in refolding guanidine **hydrochloride** -treated malate dehydrogenase to its native state. Our findings indicate that the positive charges on R21, R49, and R103 are important determinants of the chaperone function of alpha A- **crystallin** and suggest that chemical modification of **arginine** residues may play a role in protein aggregation during lens aging and cataract formation.
Identifiers--KeyWord Plus(R): HEAT-SHOCK-PROTEIN; HUMAN LENS PROTEINS; B-**CRYSTALLIN** ; MOLECULAR CHAPERONE; MAILLARD REACTION; CROSS-LINKS; POSTTRANSLATIONAL MODIFICATIONS; OLIGOMERIC SIZE; SERUM-ALBUMIN; GLYCATION
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WYATT PJ, 1993, V272, P1, ANAL CHIM ACTA

Title: Effect of site-directed mutagenesis of methylglyoxal-modifiable arginine **residues on the structure and chaperone function of human alpha A-** crystallin

Abstract: We reported previously that chemical modification of human alpha A- **crystallin** by a metabolic dicarbonyl compound, methylglyoxal (MGO), enhances its chaperone-like function, a phenomenon which we attributed to formation of argpyrimidine at **arginine** residues (R) 21 49, and 103. This structural change removes the positive charge on the **arginine** residues. To explore this mechanism further, we replaced these three R residues with a neutral...

...aromatic amino acid residues in mutant proteins. When compared to wild-type (wt) alpha A- **crystallin** , the chaperone function of R21A and R103A mutants increased 20% and 18% as measured by...

...in these assays. R21A and R103A mutants had higher surface hydrophobicity than wt alpha A- **crystallin** , but the R49A mutant had lower hydrophobicity. R21A and R103A mutants, but not the R49A mutant, were more efficient than wt protein in refolding guanidine **hydrochloride** -treated malate dehydrogenase to its native state. Our findings indicate that the positive charges on R21, R49, and R103 are important determinants of the chaperone function of alpha A- **crystallin** and suggest that chemical modification of **arginine** residues may play a role in protein aggregation during lens aging and cataract formation.

...Identifiers--HEAT-SHOCK-PROTEIN; HUMAN LENS PROTEINS; B- **CRYSTALLIN** ; MOLECULAR CHAPERONE; MAILLARD REACTION; CROSS-LINKS; POSTTRANSLATIONAL MODIFICATIONS; OLIGOMERIC SIZE; SERUM-ALBUMIN; GLYCATION

9/9,K/5 (Item 2 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

14246175 Genuine Article#: 953HG Number of References: 44

Title: Modulation of alpha- crystallin **chaperone activity in diabetic rat lens by curcumin**

Author(s): Kumar PA; Suryanarayana P; Reddy PY; Reddy GB (REPRINT)

Corporate Source: Natl Inst Nutr,Hyderabad 500007/Andhra Pradesh/India/ (REPRINT); Natl Inst Nutr,Hyderabad 500007/Andhra Pradesh/India/(geereddy@yahoo.com)

Journal: MOLECULAR VISION, 2005, V11, N66 (JUL 26), P561-568

ISSN: 1090-0535 Publication date: 20050726

Publisher: MOLECULAR VISION, C/O JEFF BOATRIGHT, LAB B, 5500 EMORY EYE CENTER, 1327 CLIFTON RD, N E, ATLANTA, GA 30322 USA

Language: English Document Type: ARTICLE

Geographic Location: India

Journal Subject Category: BIOCHEMISTRY & MOLECULAR BIOLOGY; OPHTHALMOLOGY

Abstract: Purpose: A decline in the chaperone-like activity of eye lens alpha- **crystallin** in diabetic conditions has been reported. In this study, we investigated whether curcumin, a dietary antioxidant, can manipulate the chaperone-like activity of alpha- **crystallin** in diabetic rat lens.

Methods: A group of rats received ip injection of streptozotocin (STZ; 35 mg/kg body weight in buffer) to induce hyperglycemia, while another group of rats received only buffer as vehicle and served as control. STZ-treated rats were assigned to 3 groups and fed either no

curcumin or 0.002% or 0.01% curcumin, respectively. Cataract progression due to hyperglycemia was monitored with a slit lamp biomicroscope. At the end of 8 weeks animals were sacrificed and lenses were collected. alpha H- and alpha L-crystallins from a set of pooled lenses in each group were isolated by gel filtration. Chaperone activity, hydrophobicity, and secondary and tertiary structure of alpha H- and alpha L-crystallins were assessed by light scattering/spectroscopic methods.

Results: A decrease in chaperone-like activity of alpha H- and alpha L-crystallins was observed in STZ-treated diabetic rats. The declined chaperone-like activity due to hyperglycemia was associated with reduced hydrophobicity and altered secondary and tertiary structure of alpha H- and alpha L-crystallins. Interestingly, alpha H- and alpha L-crystallins isolated from curcumin fed diabetic rat lenses had shown improved chaperone-like activity as compared to alpha H- and alpha L-crystallins from untreated diabetic rat lens. Feeding of curcumin prevented the alterations in hydrophobicity and structural changes due to STZ-induced hyperglycemia. Modulation of functional and structural properties by curcumin was found to be greater with the alpha L- **crystallin** than alpha H- **crystallin** . Loss of chaperone activity of alpha- **crystallin** , particularly alpha L- **crystallin** , in diabetic rat lens could be attributed at least partly to increased oxidative stress. Being an antioxidant, curcumin feeding has prevented the loss of alpha- **crystallin** chaperone activity and delayed the progression and maturation of diabetic cataract.

Conclusions: We demonstrate that curcumin, at the levels close to dietary consumption, prevented the loss of chaperone-like activity of alpha- **crystallin** vis-a-vis cataractogenesis due to diabetes in rat lens.

Identifiers--KeyWord Plus(R): A- **CRYSTALLIN** ; B- **CRYSTALLIN** ; **ARGININE HYDROCHLORIDE** ; IN-VIVO; CATARACT; AGGREGATION; PROTECT; STRESS; INDIA; RISK

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YANG FS, 2005, V280, P5892, J BIOL CHEM

Title: Modulation of alpha- crystallin **chaperone activity in diabetic rat lens by curcumin**

Abstract: Purpose: A decline in the chaperone-like activity of eye lens alpha- **crystallin** in diabetic conditions has been reported. In this study, we investigated whether curcumin, a dietary antioxidant, can manipulate the chaperone-like activity of alpha- **crystallin** in diabetic rat lens.

Methods: A group of rats received ip injection of streptozotocin (STZ...

...functional and structural properties by curcumin was found to be greater with the alpha L- **crystallin** than alpha H- **crystallin** . Loss of chaperone activity of alpha- **crystallin** , particularly alpha L- **crystallin** , in diabetic rat lens could be attributed at least partly to increased oxidative stress. Being an antioxidant, curcumin feeding has prevented the loss of alpha- **crystallin** chaperone activity and delayed the progression and maturation of diabetic cataract.

Conclusions: We demonstrate that...

...the levels close to dietary consumption, prevented the loss of chaperone-like activity of alpha- **crystallin** vis-a-vis cataractogenesis due to diabetes in rat lens.

...Identifiers--A- **CRYSTALLIN** ; B- **CRYSTALLIN** ; **ARGININE HYDROCHLORIDE** ; IN-VIVO; CATARACT; AGGREGATION; PROTECT; STRESS; INDIA; RISK

? t s9/9,k/11-20

9/9,K/11 (Item 8 from file: 34)

05732997 Genuine Article#: WU248 Number of References: 41

Title: Modulation of endogenous antioxidant enzymes by nitric oxide in rat C-6 glial cells

Author(s): Dobashi K; Pahan K; Chahal A; Singh I (REPRINT)
Corporate Source: MED UNIV S CAROLINA,DEPT PEDIAT, DIV DEV NEUROGENET, 171 ASHLEY AVE/CHARLESTON//SC/29425 (REPRINT); MED UNIV S CAROLINA,DEPT PEDIAT, DIV DEV NEUROGENET/CHARLESTON//SC/29425

Journal: JOURNAL OF NEUROCHEMISTRY, 1997, V68, N5 (MAY), P1896-1903
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Journal Subject Category: BIOCHEMISTRY & MOLECULAR BIOLOGY; NEUROSCIENCES

Abstract: To understand the possible mechanism of nitric oxide (NO)-mediated cytotoxicity, we investigated the effect of NO on the endogenous antioxidant enzymes (AOEs) catalase, glutathione peroxidase (GPX), and CuZn- and Mn-superoxide dismutases (SODs) in rat C-6 glial cells under conditions in which these cells expressed oligodendrocyte-like properties as evidenced by the expression of 2',3'-cyclic-nucleotide 3'-phosphohydrolase. The 24-h treatment with S-nitroso-N-acetylpenicillamine (SNAP), a NO donor, decreased the activities and the protein levels of catalase, GPX, and Mn-SOD in a dose-dependent manner. Alternatively, the activity and the protein level of CuZn-SOD were increased. 2-Phenyl-4,4, 5,5-tetramethylimidazoline-1-oxyl-3-oxide (PTIO), a NO scavenger, blocked the effect of SNAP. Moreover, the treatment of C-6 cells with sodium nitroprusside, another NO donor, or with a combination of lipopolysaccharide (LPS) and interferon-gamma (IFN-gamma), which induce excessive production of NO, also significantly modulated the AOE activities in a manner similar to that seen with SNAP treatment. The compounds/enzymes that inhibit the production of NO (e.g., N-nitro-L-**arginine** methyl ester **hydrochloride** , arginase, and PTIO) blocked the effects of LPS and IFN-gamma on the activities of AOEs. Treatment with SNAP and a combination of LPS and IFN-gamma also modulated the mRNA levels of AOEs, parallel to the changes in their protein levels and activities, except for Mn-SOD where the combination of LPS and IFN-gamma markedly stimulated the mRNA expression. In spite of the stimulation of mRNA level, LPS and IFN-gamma significantly inhibited the activity of Mn-SOD within the first 24 h of incubation; however, Mn-SOD activity gradually increased with the increase in time of incubation. These results suggest that alterations in the status of AOEs by NO may be the basis of NO-induced cytotoxicity in disease states associated with excessive NO production.

Descriptors--Author Keywords: nitric oxide ; cytokine ; glia ; antioxidant enzymes ; gene expression
Identifiers--KeyWord Plus(R): SUPEROXIDE-DISMUTASE; REVERSIBLE BINDING; SYNTHASE ACTIVITY; INDUCTION; INHIBITION; MECHANISM; PEROXYNITRITE; CYTOTOXICITY; EXPRESSION; PROTEIN
Research Fronts: 95-2212 003 (PEROXYNITRITE IN-VITRO; NITRIC-OXIDE SYNTHASE; HYDROXYL RADICAL; FORMATION OF 8-NITROGUANINE; PC12 CELLS)
95-2984 001 (INDUCIBLE NITRIC-OXIDE SYNTHASE; CULTURED RAT ASTROCYTES; INCREASED EXPRESSION OF NADPH DIAPHORASE)
95-3190 001 (INCREASED ABUNDANCE OF SPECIFIC SKELETAL-MUSCLE PROTEIN-TYROSINE PHOSPHATASES; ALPHA-B- **CRYSTALLIN** EXPRESSION)
95-3891 001 (IN-VITRO TUMOR-NECROSIS-FACTOR CYTOTOXICITY; TRANSFECTION OF CELLS; MANGANESE SUPEROXIDE-DISMUTASE; GENE-EXPRESSION FOR

IMMUNOMODULATING CYTOKINES)
95-6776 001 (INDUCIBLE NITRIC-OXIDE SYNTHASE; RAT MACROPHAGES MEDIATE FUNGISTATIC ACTIVITY; MICROGLIAL RELEASE)
95-8090 001 (NITRIC-OXIDE SYNTHASE; INCREASED INTRACELLULAR CA2+ SELECTIVELY SUPPRESSES IL-1-INDUCED NO PRODUCTION; HUMAN CENTRAL-NERVOUS-SYSTEM TUMORS)

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...Abstract: treatment. The compounds/enzymes that inhibit the production of NO (e.g., N-nitro-L- **arginine** methyl ester **hydrochloride** , arginase, and PTIO) blocked the effects of LPS and IFN-gamma on the activities of...

...Research Fronts: DIAPHORASE)
95-3190 001 (INCREASED ABUNDANCE OF SPECIFIC SKELETAL-MUSCLE PROTEIN-TYROSINE PHOSPHATASES; ALPHA-B- **CRYSTALLIN** EXPRESSION)
95-3891 001 (IN-VITRO TUMOR-NECROSIS-FACTOR CYTOTOXICITY; TRANSFECTION

OF CELLS; MANGANESE SUPEROXIDE...

9/9,K/12 (Item 1 from file: 35)
DIALOG(R)File 35:Dissertation Abs Online

02045668 ORDER NO: AADAA-INQ94247
Intragenic complementation and protein oligomerization studies in argininosuccinate lyase and its homologue delta crystallin
Author: Yu, Bomina
Degree: Ph.D.
Year: 2004
Corporate Source/Institution: University of Toronto (Canada) (0779)
Advisers: P. L. Honell; A. R. Davidson
Source: VOLUME 65/10-B OF DISSERTATION ABSTRACTS INTERNATIONAL.
PAGE 5140. 261 PAGES
Descriptors: CHEMISTRY, BIOCHEMISTRY
Descriptor Codes: 0487
ISBN: 0-612-94247-3

<?Pub Inc> Argininosuccinate lyase (ASL) is a ubiquitous enzyme that catalyzes the reversible cleavage of argininosuccinate to **arginine** and fumarate. This reaction is important both for the detoxification of ammonia <italic>via</italic> the urea cycle and for the biosynthesis of **arginine** . Through a process called 'gene sharing' ASL was recruited to the eye lens of birds and reptiles where it acts as the major lens **crystallin** . Both ASL and δ **crystallin** exist as homotetramers with a monomer molecular weight of approximately 50 kDa. Extensive intragenic complementation was observed at the ASL locus in humans. Intragenic complementation occurs when certain combinations of mutant alleles produce an enzyme with greater catalytic activity than is observed in the homozygous state of either mutant.

In this thesis, ASL and δ2 **crystallin** were used as model systems to study intragenic complementation and protein oligomerization. The structure and function of mutant proteins possessing amino acid substitutions associated with ASL deficiency were characterized. Mutations were found to either disturb the active site or drastically destabilize the protein such that proper metabolic function would be compromised. By coexpressing different pairs of mutants, intragenic complementation was found to occur between two active site mutants by the regeneration of native-like active sites and between stable and unstable mutants due to the increase in stability upon oligomerization. Complementation was also observed between δ2 **crystallin** mutants and between δ2 **crystallin** and ASL, implying that ASL and δ2 **crystallin** have similar subunit interfaces and that the two proteins fold in the same manner. Both proteins were found to unfold in guanidine **hydrochloride** <italic>via</italic> a partially folded dimeric intermediate. Extensive site-directed mutagenesis at the subunit interface and of residues buried in the monomer suggested that unfolding occurs independent of the oligomeric state and illustrated the importance of inter-subunit salt-bridges for maintaining tetramer stability. Intragenic complementation was observed between mutant proteins with opposite amino acid substitutions in the subunit interface. Together these studies have provided insight into the pathology of argininosuccinic aciduria and the folding mechanism of ASL and δ2 **crystallin** , and have illustrated the value of intragenic complementation studies when examining subunit interactions in oligomeric

proteins.

Intragenic complementation and protein oligomerization studies in argininosuccinate lyase and its homologue delta crystallin

...Argininosuccinate lyase (ASL) is a ubiquitous enzyme that catalyzes the reversible cleavage of argininosuccinate to **arginine** and fumarate. This reaction is important both for the detoxification of ammonia <italic>via</italic> the urea cycle and for the biosynthesis of **arginine** . Through a process called 'gene sharing' ASL was recruited to the eye lens of birds and reptiles where it acts as the major lens **crystallin** . Both ASL and δ **crystallin** exist as homotetramers with a monomer molecular weight of approximately 50 kDa. Extensive intragenic complementation...
...observed in the homozygous state of either mutant.
In this thesis, ASL and δ2 **crystallin** were used as model systems to study intragenic complementation and protein oligomerization. The structure and...

...due to the increase in stability upon oligomerization. Complementation was also observed between δ2 **crystallin** mutants and between δ2 **crystallin** and ASL, implying that ASL and δ2 **crystallin** have similar subunit interfaces and that the two proteins fold in the same manner. Both proteins were found to unfold in guanidine **hydrochloride** <italic>via</italic> a partially folded dimeric intermediate. Extensive site-directed mutagenesis at the subunit...

...into the pathology of argininosuccinic aciduria and the folding mechanism of ASL and δ2 **crystallin** , and have illustrated the value of intragenic complementation studies when examining subunit interactions in oligomeric...

9/9,K/13 (Item 1 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE

03320778 2006097921
Effect of site-directed mutagenesis of methylglyoxal-modifiable arginine **residues on the structure and chaperone function of human alphaA-** crystallin
Biswas A.; Miller A.; Oya-Ito T.; Santhoshkumar P.; Bhat M.; Nagaraj R.H.
ADDRESS: R.H. Nagaraj, Department of Ophthalmology, Case Western Reserve University, Cleveland, OH 44106, United States
EMAIL: ram.nagaraj@case.edu
Journal: Biochemistry, 45/14 (4569-4577), 2006, United States
PUBLICATION DATE: April 11, 2006
CODEN: BICHA
ISSN: 0006-2960
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LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 59

We reported previously that chemical modification of human alphaA-**crystallin** by a metabolic dicarbonyl compound, methylglyoxal (MGO), enhances its chaperone-like function, a phenomenon which we attributed to formation of argpyrimidine at **arginine** residues (R) 21, 49, and 103. This

structural change removes the positive charge on the **arginine** residues. To explore this mechanism further, we replaced these three R residues with a neutral alanine (A) residue one at a time or in combination and examined the impact on the structure and chaperone function. Measurement of intrinsic tryptophan fluorescence and near-UV CD spectra revealed alteration of the microenvironment of aromatic amino acid residues in mutant proteins. When compared to wild-type (wt) alphaA- **crystallin** , the chaperone function of R21A and R103A mutants increased 20% and 18% as measured by the insulin aggregation assay and increased it as much as 39% and 28% when measured by the citrate synthase (CS) aggregation assay. While the R49A mutant lost most of its chaperone function, R21A/R103A and R21A/R49A/R103A mutants had slightly better function (6-14% and 10-14%) than the wt protein in these assays. R21A and R103A mutants had higher surface hydrophobicity than wt alphaA- **crystallin** , but the R49A mutant had lower hydrophobicity. R21A and R103A mutants, but not the R49A mutant, were more efficient than wt protein in refolding guanidine **hydrochloride** -treated malate dehydrogenase to its native state. Our findings indicate that the positive charges on R21, R49, and R103 are important determinants of the chaperone function of alphaA- **crystallin** and suggest that chemical modification of **arginine** residues may play a role in protein aggregation during lens aging and cataract formation. (c) 2006 American Chemical Society.

CLASSIFICATION CODE AND DESCRIPTION:

82.3.6 - PROTEIN BIOCHEMISTRY / PROTEIN ENGINEERING / Mutation, Expression and Isolation

82.2.8 - PROTEIN BIOCHEMISTRY / STRUCTURAL STUDIES / Folding, Unfolding and Stability

82.2.3 - PROTEIN BIOCHEMISTRY / STRUCTURAL STUDIES / Protein Crystallization and Crystal Structures

Effect of site-directed mutagenesis of methylglyoxal-modifiable arginine **residues on the structure and chaperone function of human alphaA-** crystallin

We reported previously that chemical modification of human alphaA- **crystallin** by a metabolic dicarbonyl compound, methylglyoxal (MGO), enhances its chaperone-like function, a phenomenon which we attributed to formation of argpyrimidine at **arginine** residues (R) 21, 49, and 103. This structural change removes the positive charge on the **arginine** residues. To explore this mechanism further, we replaced these three R residues with a neutral...

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9/9,K/14 (Item 2 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE

02344455 2003128140
Structural perturbation and enhancement of the chaperone-like activity of alpha- crystallin by arginine hydrochloride
Srinivas V.; Raman B.; Rao K.S.; Ramakrishna T.; Rao Ch.M.
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EMAIL: mohan@ccmb.res.in
Journal: Protein Science, 12/6 (1262-1270), 2003, United States
PUBLICATION DATE: June 1, 2003
CODEN: PRCIE
ISSN: 0961-8368
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 57

Structural perturbation of alpha- **crystallin** is shown to enhance its molecular chaperone-like activity in preventing aggregation of target proteins. We demonstrate that **arginine** , a biologically compatible molecule that is known to bind to the peptide backbone and negatively charged side-chains, increases the chaperone-like activity of calf eye lens alpha- **crystallin** as well as recombinant human alphaA- and alphaB-crystallins. Arginineinduced increase in the chaperone activity is more pronounced for alphaB- **crystallin** than for alphaA- **crystallin** . Other guanidinium compounds such as aminoguanidine **hydrochloride** and guanidine **hydrochloride** also show a similar effect, but to different extents. A point mutation, R120G, in alphaB- **crystallin** that is associated with desmin-related myopathy, results in a significant loss of chaperone-like activity. **Arginine** restores the activity of mutant protein to a considerable extent. We have investigated the effect of **arginine** on the structural changes of alpha- **crystallin** by circular dichroism, fluorescence, and glycerol gradient sedimentation. Far-UV CD spectra show no significant changes in secondary structure, whereas near-UV CD spectra show subtle changes in the presence of **arginine** . Glycerol gradient sedimentation shows a significant decrease in the size of alpha- **crystallin** oligomer in the presence of **arginine** . Increased exposure of hydrophobic surfaces of alpha- **crystallin** , as monitored by pyrene-solubilization and ANS-fluorescence, is observed in the presence of **arginine** . These results show that **arginine** brings about subtle changes in the tertiary structure and significant changes in the quaternary structure of alpha- **crystallin** and enhances its chaperone-like activity significantly. This study should prove useful in designing strategies to improve chaperone function for therapeutic applications.
DESCRIPTORS:
Chaperone-like activity; alpha- **crystallin** ; **Arginine** ; Aminoguanidine; Structural perturbation

CLASSIFICATION CODE AND DESCRIPTION:
82.2.8 - PROTEIN BIOCHEMISTRY / STRUCTURAL STUDIES / Folding, Unfolding and Stability

Structural perturbation and enhancement of the chaperone-like activity of alpha- crystallin by arginine hydrochloride

Structural perturbation of alpha- **crystallin** is shown to enhance its molecular chaperone-like activity in preventing aggregation of target proteins. We demonstrate that **arginine** , a biologically compatible molecule that is known to bind to the peptide backbone and negatively charged side-chains, increases the chaperone-like activity of calf eye lens alpha- **crystallin** as well as recombinant human alphaA- and alphaB-crystallins. Arginineinduced increase in the chaperone activity is more pronounced for alphaB- **crystallin** than for alphaA- **crystallin** . Other guanidinium compounds such as aminoguanidine **hydrochloride** and guanidine **hydrochloride** also show a similar effect, but to different extents. A point mutation, R120G, in alphaB- **crystallin** that is associated with desmin-related myopathy, results in a significant loss of chaperone-like activity. **Arginine** restores the activity of mutant protein to a considerable extent. We have investigated the effect of **arginine** on the structural changes of alpha- **crystallin** by circular dichroism, fluorescence, and glycerol gradient sedimentation. Far-UV CD spectra show no significant...

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DESCRIPTORS:
Chaperone-like activity; alpha- **crystallin** ; **Arginine** ; Aminoguanidine; Structural perturbation

9/9,K/15 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

13754273 EMBASE No: 2006169408
Effect of site-directed mutagenesis of methylglyoxal-modifiable arginine **residues on the structure and chaperone function of human alphaA-**crystallin
Biswas A.; Miller A.; Oya-Ito T.; Santhoshkumar P.; Bhat M.; Nagaraj R.H.
R.H. Nagaraj, Department of Ophthalmology, Case Western Reserve University, Cleveland, OH 44106 United States
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Biochemistry (BIOCHEMISTRY) (United States) 11 APR 2006, 45/14 (4569-4577)
CODEN: BICHA ISSN: 0006-2960
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 59

We reported previously that chemical modification of human alphaA-**crystallin** by a metabolic dicarbonyl compound, methylglyoxal (MGO), enhances its chaperone-like function, a phenomenon which we attributed to formation of argpyrimidine at **arginine** residues (R) 21, 49, and 103. This

structural change removes the positive charge on the **arginine** residues. To explore this mechanism further, we replaced these three R residues with a neutral alanine (A) residue one at a time or in combination and examined the impact on the structure and chaperone function. Measurement of intrinsic tryptophan fluorescence and near-UV CD spectra revealed alteration of the microenvironment of aromatic amino acid residues in mutant proteins. When compared to wild-type (wt) alphaA- **crystallin** , the chaperone function of R21A and R103A mutants increased 20% and 18% as measured by the insulin aggregation assay and increased it as much as 39% and 28% when measured by the citrate synthase (CS) aggregation assay. While the R49A mutant lost most of its chaperone function, R21A/R103A and R21A/R49A/R103A mutants had slightly better function (6-14% and 10-14%) than the wt protein in these assays. R21A and R103A mutants had higher surface hydrophobicity than wt alphaA- **crystallin** , but the R49A mutant had lower hydrophobicity. R21A and R103A mutants, but not the R49A mutant, were more efficient than wt protein in refolding guanidine **hydrochloride** -treated malate dehydrogenase to its native state. Our findings indicate that the positive charges on R21, R49, and R103 are important determinants of the chaperone function of alphaA- **crystallin** and suggest that chemical modification of **arginine** residues may play a role in protein aggregation during lens aging and cataract formation. (c) 2006 American Chemical Society.

DRUG DESCRIPTORS:
*alpha **crystallin** ; *methylglyoxal; * **arginine**
chaperone; pyrimidine; amino acid; citrate synthase; mutant protein; guanidine **hydrochloride** ; insulin; malate dehydrogenase; aromatic amino acid
MEDICAL DESCRIPTORS:
*protein structure; *site directed mutagenesis; *protein function
protein modification; circular dichroism; amino acid substitution; hydrophobicity; protein folding; cataractogenesis; protein aggregation; aging; lens; human; controlled study; article; priority journal
CAS REGISTRY NO.: 78-98-8 (methylglyoxal); 1119-34-2, 15595-35-4, 7004-12-8 , 74-79-3 (**arginine**); 289-95-2 (pyrimidine); 65072-01-7 (amino acid); 9027-96-7 (citrate synthase); 50-01-1 (guanidine **hydrochloride**); 9004-10-8 (insulin); 9001-64-3 (malate dehydrogenase)
SECTION HEADINGS:
012 Ophthalmology
029 Clinical and Experimental Biochemistry

Effect of site-directed mutagenesis of methylglyoxal-modifiable arginine **residues on the structure and chaperone function of human alphaA-** crystallin

We reported previously that chemical modification of human alphaA- **crystallin** by a metabolic dicarbonyl compound, methylglyoxal (MGO), enhances its chaperone-like function, a phenomenon which we attributed to formation of argpyrimidine at **arginine** residues (R) 21, 49, and 103. This structural change removes the positive charge on the **arginine** residues. To explore this mechanism further, we replaced these three R residues with a neutral...

...of aromatic amino acid residues in mutant proteins. When compared to wild-type (wt) alphaA- **crystallin** , the chaperone function of R21A and R103A mutants increased 20% and 18% as measured by...

...protein in these assays. R21A and R103A mutants had higher surface hydrophobicity than wt alphaA- **crystallin** , but the R49A mutant had lower hydrophobicity. R21A and R103A mutants, but not the R49A mutant, were more efficient than wt protein in refolding guanidine **hydrochloride** -treated malate dehydrogenase to its native state. Our findings indicate that the positive charges on R21, R49, and R103 are important determinants of the chaperone function of alphaA- **crystallin** and suggest that chemical modification of **arginine** residues may play a role in protein aggregation during lens aging and cataract formation. (c...
DRUG DESCRIPTORS:
*alpha **crystallin** ; *methylglyoxal; * **arginine**
chaperone; pyrimidine; amino acid; citrate synthase; mutant protein; guanidine **hydrochloride** ; insulin; malate dehydrogenase; aromatic amino acid
...CAS REGISTRY NO.: 74-79-3 (**arginine**); 289-95-2 (pyrimidine); 65072-01-7 (amino acid); 9027-96-7 (citrate synthase); 50-01-1 (guanidine **hydrochloride**); 9004-10-8 (insulin); 9001-64-3 (malate dehydrogenase)

9/9,K/16 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

13357267 EMBASE No: 2005431360
Arginine hydrochloride **enhances the dynamics of subunit assembly and the chaperone-like activity of alpha-** crystallin
Srinivas V.; Raman B.; Sridhar Rao K.; Ramakrishna T.; Mohan Rao Ch.
Dr. Ch. Mohan Rao, Centre for Cellular and Molecular Biology, Uppal Road, Hyderabad 500 007 India
AUTHOR EMAIL: mohan@ccmb.res.in
Molecular Vision (MOL. VISION) (United States) 01 APR 2005, 11/- (249-255)
CODEN: MVEPF ISSN: 1090-0535
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 49

Purpose: alpha- **Crystallin** , a major eye lens protein, bears homology with small heat shock proteins (sHsps) and exhibits molecular chaperone-like activity. Structural perturbation by temperature or low concentrations of denaturants leads to enhancement of its chaperone-like activity. We have earlier demonstrated similar enhancement of chaperone-like activity using biologically compatible solutes such as **arginine** **hydrochloride** and aminoguanidine. The purpose of the present study is to get an insight into the mechanism of the **arginine** induced enhancement of chaperone-like activity of **crystallin** . Methods: The effect of **arginine** **hydrochloride** on the chaperone-like activity of alpha- **crystallin** at 25 degreesC was studied using DTT induced aggregation of insulin as a model system. Changes in the accessibility of the thiol group near the end of the a- **crystallin** domain in the absence and the presence of **arginine** **hydrochloride** were studied using dithiobisnitrobenzoic acid. Fluorescence resonance energy transfer studies were performed to investigate changes in the dynamics of the subunit assembly. Urea induced denaturation studies of alpha- **crystallin** were carried out to investigate structural destabilization of alpha- **crystallin** , if any, in the presence of **arginine** **hydrochloride** . Results: **Arginine** **hydrochloride**

increases the chaperone-like activity of alpha- **crystallin** several fold towards DTT induced aggregation of insulin at room temperature. Our study shows that both the extent and the rate of accessibility of the thiol group are increased in the presence of **arginine** . Fluorescence resonance energy transfer experiments show that **arginine** **hydrochloride** significantly increases the subunit exchange between the oligomers of alpha- **crystallin** . **Arginine** induced structural perturbation and loosening of subunit assembly of alpha- **crystallin** leads to overall destabilization of the protein as reflected by the urea denaturation study. Conclusions: **Arginine** perturbs the tertiary and quaternary structure of a- **crystallin** and enhances the dynamics of the subunit assembly leading to enhanced chaperone-like activity. Thus, in addition to size, surface hydrophobicity, and charge distribution, the dynamics of the subunit assembly appears to be one of the critical factors that can modulate the chaperone activity.

DRUG DESCRIPTORS:
* **arginine** ; *chaperone; *alpha **crystallin**
dithiothreitol; insulin; benzoic acid; urea
MEDICAL DESCRIPTORS:
protein assembly; biological model; protein domain; fluorescence resonance energy transfer; protein denaturation; protein structure; room temperature; hydrophobicity; article; priority journal
CAS REGISTRY NO.: 1119-34-2, 15595-35-4, 7004-12-8, 74-79-3 (**arginine**); 3483-12-3 (dithiothreitol); 9004-10-8 (insulin); 532-32-1, 582-25-2, 65-85-0, 766-76-7 (benzoic acid); 57-13-6 (urea)
SECTION HEADINGS:
029 Clinical and Experimental Biochemistry

Arginine hydrochloride **enhances the dynamics of subunit assembly and the chaperone-like activity of alpha-** crystallin
Purpose: alpha- **Crystallin** , a major eye lens protein, bears homology with small heat shock proteins (sHsps) and exhibits...

...have earlier demonstrated similar enhancement of chaperone-like activity using biologically compatible solutes such as **arginine** **hydrochloride** and aminoguanidine. The purpose of the present study is to get an insight into the mechanism of the **arginine** induced enhancement of chaperone-like activity of **crystallin** . Methods: The effect of **arginine** **hydrochloride** on the chaperone-like activity of alpha- **crystallin** at 25 degreesC was studied using DTT induced aggregation of insulin as a model system. Changes in the accessibility of the thiol group near the end of the a- **crystallin** domain in the absence and the presence of **arginine** **hydrochloride** were studied using dithiobisnitrobenzoic acid. Fluorescence resonance energy transfer studies were performed to investigate changes in the dynamics of the subunit assembly. Urea induced denaturation studies of alpha- **crystallin** were carried out to investigate structural destabilization of alpha- **crystallin** , if any, in the presence of **arginine** **hydrochloride** . Results: **Arginine** **hydrochloride** increases the chaperone-like activity of alpha- **crystallin** several fold towards DTT induced aggregation of insulin at room temperature. Our study shows that...

...and the rate of accessibility of the thiol group are increased in the presence of **arginine** . Fluorescence resonance energy transfer experiments show that **arginine** **hydrochloride** significantly increases the subunit exchange between the oligomers of alpha- **crystallin** . **Arginine** induced structural perturbation and loosening of subunit assembly of alpha-

crystallin leads to overall destabilization of the protein as reflected by the urea denaturation study. Conclusions: **Arginine** perturbs the tertiary and quaternary structure of a- **crystallin** and enhances the dynamics of the subunit assembly leading to enhanced chaperone-like activity. Thus...
DRUG DESCRIPTORS:
* **arginine** ; *chaperone; *alpha **crystallin**
...CAS REGISTRY NO.: 74-79-3 (**arginine**); 3483-12-3 (dithiothreitol); 9004-10-8 (insulin); 532-32-1...

9/9,K/17 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

12095641 EMBASE No: 2003207170
Structural perturbation and enhancement of the chaperone-like activity of alpha- crystallin **by** arginine hydrochloride
Srinivas V.; Raman B.; Rao K.S.; Ramakrishna T.; Rao Ch.M.
Ch.M. Rao, Ctr. for Cell. and Molecular Biology, Uppal Road, Hyderabad 500 007 India
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Protein Science (PROTEIN SCI.) (United States) 01 JUN 2003, 12/6 (1262-1270)
CODEN: PRCIE ISSN: 0961-8368
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 57

Structural perturbation of alpha- **crystallin** is shown to enhance its molecular chaperone-like activity in preventing aggregation of target proteins. We demonstrate that **arginine** , a biologically compatible molecule that is known to bind to the peptide backbone and negatively charged side-chains, increases the chaperone-like activity of calf eye lens alpha- **crystallin** as well as recombinant human alphaA- and alphaB-crystallins. Arginineinduced increase in the chaperone activity is more pronounced for alphaB- **crystallin** than for alphaA- **crystallin** . Other guanidinium compounds such as aminoguanidine **hydrochloride** and guanidine **hydrochloride** also show a similar effect, but to different extents. A point mutation, R120G, in alphaB- **crystallin** that is associated with desmin-related myopathy, results in a significant loss of chaperone-like activity. **Arginine** restores the activity of mutant protein to a considerable extent. We have investigated the effect of **arginine** on the structural changes of alpha- **crystallin** by circular dichroism, fluorescence, and glycerol gradient sedimentation. Far-UV CD spectra show no significant changes in secondary structure, whereas near-UV CD spectra show subtle changes in the presence of **arginine** . Glycerol gradient sedimentation shows a significant decrease in the size of alpha- **crystallin** oligomer in the presence of **arginine** . Increased exposure of hydrophobic surfaces of alpha- **crystallin** , as monitored by pyrene-solubilization and ANS-fluorescence, is observed in the presence of **arginine** . These results show that **arginine** brings about subtle changes in the tertiary structure and significant changes in the quaternary structure of alpha- **crystallin** and enhances its chaperone-like activity significantly. This study should prove useful in designing strategies to improve chaperone function for therapeutic applications.

DRUG DESCRIPTORS:

*chaperone; *alpha **crystallin** --endogenous compound--ec; * **arginine** guanidine derivative; aminoguanidine; guanidine **hydrochloride** ; desmin; glycerol; pyrene; oligomer; unclassified drug
MEDICAL DESCRIPTORS:
*protein structure
structure analysis; protein targeting; protein binding; point mutation; circular dichroism; fluorescence; sedimentation; protein secondary structure; solubilization; protein tertiary structure; protein quaternary structure; nonhuman; article; priority journal
DRUG TERMS (UNCONTROLLED): alpha b **crystallin**
CAS REGISTRY NO.: 1119-34-2, 15595-35-4, 7004-12-8, 74-79-3 (**arginine**); 1068-42-4, 2582-30-1, 79-17-4 (aminoguanidine); 50-01-1 (guanidine **hydrochloride**); 56-81-5 (glycerol); 129-00-0 (pyrene)
SECTION HEADINGS:
029 Clinical and Experimental Biochemistry

Structural perturbation and enhancement of the chaperone-like activity of alpha- crystallin **by** arginine hydrochloride

Structural perturbation of alpha- **crystallin** is shown to enhance its molecular chaperone-like activity in preventing aggregation of target proteins. We demonstrate that **arginine** , a biologically compatible molecule that is known to bind to the peptide backbone and negatively charged side-chains, increases the chaperone-like activity of calf eye lens alpha- **crystallin** as well as recombinant human alphaA- and alphaB-crystallins. Arginineinduced increase in the chaperone activity is more pronounced for alphaB- **crystallin** than for alphaA- **crystallin** . Other guanidinium compounds such as aminoguanidine **hydrochloride** and guanidine **hydrochloride** also show a similar effect, but to different extents. A point mutation, R120G, in alphaB- **crystallin** that is associated with desmin-related myopathy, results in a significant loss of chaperone-like activity. **Arginine** restores the activity of mutant protein to a considerable extent. We have investigated the effect of **arginine** on the structural changes of alpha- **crystallin** by circular dichroism, fluorescence, and glycerol gradient sedimentation. Far-UV CD spectra show no significant...

...in secondary structure, whereas near-UV CD spectra show subtle changes in the presence of **arginine** . Glycerol gradient sedimentation shows a significant decrease in the size of alpha- **crystallin** oligomer in the presence of **arginine** . Increased exposure of hydrophobic surfaces of alpha- **crystallin** , as monitored by pyrene-solubilization and ANS-fluorescence, is observed in the presence of **arginine** . These results show that **arginine** brings about subtle changes in the tertiary structure and significant changes in the quaternary structure of alpha- **crystallin** and enhances its chaperone-like activity significantly. This study should prove useful in designing strategies...
DRUG DESCRIPTORS:
*chaperone; *alpha **crystallin** --endogenous compound--ec; * **arginine** guanidine derivative; aminoguanidine; guanidine **hydrochloride** ; desmin; glycerol; pyrene; oligomer; unclassified drug
DRUG TERMS (UNCONTROLLED): alpha b **crystallin**
...CAS REGISTRY NO.: 74-79-3 (**arginine**); 1068-42-4...

...79-17-4 (aminoguanidine); 50-01-1 (guanidine **hydrochloride**); 56-81-5 (glycerol); 129-00-0 (pyrene)

9/9,K/18 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

20818450 PMID: 16584192

Effect of site-directed mutagenesis of methylglyoxal-modifiable arginine **residues on the structure and chaperone function of human alphaA-** crystallin .

Biswas Ashis; Miller Antonia; Oya-Ito Tomoko; Santhoshkumar Puttur; Bhat Manjunatha; Nagaraj Ram H

Department of Ophthalmology, Case Western Reserve University, Cleveland, Ohio 44106, USA.

Biochemistry (United States) Apr 11 2006, 45 (14) p4569-77, ISSN 0006-2960--Print Journal Code: 0370623

Contract/Grant No.: P30EY-11373; EY; NEI; R01EY-016219; EY; NEI; R01EY-09912; EY; NEI

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Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS; Toxbib

We reported previously that chemical modification of human alphaA- **crystallin** by a metabolic dicarbonyl compound, methylglyoxal (MGO), enhances its chaperone-like function, a phenomenon which we attributed to formation of argpyrimidine at **arginine** residues (R) 21, 49, and 103. This structural change removes the positive charge on the **arginine** residues. To explore this mechanism further, we replaced these three R residues with a neutral alanine (A) residue one at a time or in combination and examined the impact on the structure and chaperone function. Measurement of intrinsic tryptophan fluorescence and near-UV CD spectra revealed alteration of the microenvironment of aromatic amino acid residues in mutant proteins. When compared to wild-type (wt) alphaA- **crystallin** , the chaperone function of R21A and R103A mutants increased 20% and 18% as measured by the insulin aggregation assay and increased it as much as 39% and 28% when measured by the citrate synthase (CS) aggregation assay. While the R49A mutant lost most of its chaperone function, R21A/R103A and R21A/R49A/R103A mutants had slightly better function (6-14% and 10-14%) than the wt protein in these assays. R21A and R103A mutants had higher surface hydrophobicity than wt alphaA- **crystallin** , but the R49A mutant had lower hydrophobicity. R21A and R103A mutants, but not the R49A mutant, were more efficient than wt protein in refolding guanidine **hydrochloride** -treated malate dehydrogenase to its native state. Our findings indicate that the positive charges on R21, R49, and R103 are important determinants of the chaperone function of alphaA- **crystallin** and suggest that chemical modification of **arginine** residues may play a role in protein aggregation during lens aging and cataract formation.

Descriptors: ***Arginine** --physiology--PH; *Molecular Chaperones --physiology--PH; *alpha- **Crystallin** A Chain--physiology--PH; **Arginine** --chemistry--CH; Carbonic Anhydrases--metabolism--ME; Circular Dichroism; Humans; Mutagenesis, Site-Directed; Protein Structure, Secondary; Pyruvaldehyde--pharmacology--PD; Research Support, N.I.H., Extramural; Research Support, Non-U.S. Gov't; Spectrometry, Fluorescence; alpha- **Crystallin** A Chain--chemistry--CH

CAS Registry No.: 0 (Molecular Chaperones); 0 (alpha-Crystallin A Chain); 74-79-3 (Arginine); 78-98-8 (Pyruvaldehyde)

Enzyme No.: EC 4.2.1.1 (Carbonic Anhydrases)
Record Date Created: 20060404
Record Date Completed: 20060530

Effect of site-directed mutagenesis of methylglyoxal-modifiable arginine **residues on the structure and chaperone function of human alphaA-** crystallin .

We reported previously that chemical modification of human alphaA- **crystallin** by a metabolic dicarbonyl compound, methylglyoxal (MGO), enhances its chaperone-like function, a phenomenon which we attributed to formation of argpyrimidine at **arginine** residues (R) 21, 49, and 103. This structural change removes the positive charge on the **arginine** residues. To explore this mechanism further, we replaced these three R residues with a neutral...

... of aromatic amino acid residues in mutant proteins. When compared to wild-type (wt) alphaA- **crystallin** , the chaperone function of R21A and R103A mutants increased 20% and 18% as measured by...

... protein in these assays. R21A and R103A mutants had higher surface hydrophobicity than wt alphaA- **crystallin** , but the R49A mutant had lower hydrophobicity. R21A and R103A mutants, but not the R49A mutant, were more efficient than wt protein in refolding guanidine **hydrochloride** -treated malate dehydrogenase to its native state. Our findings indicate that the positive charges on R21, R49, and R103 are important determinants of the chaperone function of alphaA- **crystallin** and suggest that chemical modification of **arginine** residues may play a role in protein aggregation during lens aging and cataract formation.

Descriptors: ***Arginine** --physiology--PH; *Molecular Chaperones --physiology--PH; *alpha- **Crystal**lin A Chain--physiology--PH; **Arginine** --chemistry--CH; Carbonic Anhydrases--metabolism--ME; Circular Dichroism; Humans; Mutagenesis, Site-Directed; Protein Structure, Secondary...

...Support, N.I.H., Extramural; Research Support, Non-U.S. Gov't; Spectrometry, Fluorescence; alpha- **Crystallin** A Chain--chemistry--CH

Chemical Name: Molecular Chaperones; alpha- **Crystallin** A Chain; **Arginine** ; Pyruvaldehyde; Carbonic Anhydrases

9/9,K/19 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

20362892 PMID: 15827547

Arginine hydrochloride **enhances the dynamics of subunit assembly and the chaperone-like activity of alpha-** crystallin .

Srinivas V; Raman B; Rao K Sridhar; Ramakrishna T; Rao Ch Mohan
Centre for Cellular and Molecular Biology, Hyderabad, India.

Molecular vision electronic resource (United States) 2005, 11 p249-55, ISSN 1090-0535--Electronic Journal Code: 9605351
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Document type: Journal Article
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Main Citation Owner: NLM
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Subfile: INDEX MEDICUS

PURPOSE: Alpha- **crystallin** , a major eye lens protein, bears homology

with small heat shock proteins (sHsps) and exhibits molecular chaperone-like activity. Structural perturbation by temperature or low concentrations of denaturants leads to enhancement of its chaperone-like activity. We have earlier demonstrated similar enhancement of chaperone-like activity using biologically compatible solutes such as **arginine hydrochloride** and aminoguanidine. The purpose of the present study is to get an insight into the mechanism of the **arginine** induced enhancement of chaperone-like activity of alpha- **crystallin** . METHODS: The effect of **arginine hydrochloride** on the chaperone-like activity of alpha- **crystallin** at 25 degrees C was studied using DTT induced aggregation of insulin as a model system. Changes in the accessibility of the thiol group near the end of the alpha- **crystallin** domain in the absence and the presence of **arginine hydrochloride** were studied using dithiobisnitrobenzoic acid. Fluorescence resonance energy transfer studies were performed to investigate changes in the dynamics of the subunit assembly. Urea induced denaturation studies of alpha- **crystallin** were carried out to investigate structural destabilization of alpha- **crystallin** , if any, in the presence of **arginine hydrochloride** . RESULTS: **Arginine hydrochloride** increases the chaperone-like activity of alpha- **crystallin** several fold towards DTT induced aggregation of insulin at room temperature. Our study shows that both the extent and the rate of accessibility of the thiol group are increased in the presence of **arginine** . Fluorescence resonance energy transfer experiments show that **arginine hydrochloride** significantly increases the subunit exchange between the oligomers of alpha- **crystallin** . **Arginine** induced structural perturbation and loosening of subunit assembly of alpha- **crystallin** leads to overall destabilization of the protein as reflected by the urea denaturation study. CONCLUSIONS: **Arginine** perturbs the tertiary and quaternary structure of alpha- **crystallin** and enhances the dynamics of the subunit assembly leading to enhanced chaperone-like activity. Thus, in addition to size, surface hydrophobicity, and charge distribution, the dynamics of the subunit assembly appears to be one of the critical factors that can modulate the chaperone activity.

Descriptors: ***Arginine** --pharmacology--PD; *Molecular Chaperones --metabolism--ME; *alpha-Crystallins--drug effects--DE; Animals; Cattle; Disulfides; Dithiothreitol; Fluorescent Dyes; Lens, Crystalline--chemistry --CH; Protein Subunits--chemistry--CH; Protein Subunits--metabolism--ME; Recombinant Proteins--chemistry--CH; Recombinant Proteins--drug effects --DE; Recombinant Proteins--metabolism--ME; Solubility; Spectrometry, Fluorescence; alpha-Crystallins--chemistry--CH; alpha-Crystallins --metabolism--ME

CAS Registry No.: 0 (Disulfides); 0 (Fluorescent Dyes); 0 (Molecular Chaperones); 0 (Protein Subunits); 0 (Recombinant Proteins); 0 (alpha-Crystallins); 3483-12-3 (Dithiothreitol); 74-79-3 (Arginine)

Record Date Created: 20050413

Record Date Completed: 20060413

Date of Electronic Publication: 20050401

Arginine hydrochloride **enhances the dynamics of subunit assembly and the chaperone-like activity of alpha-** crystallin .

PURPOSE: Alpha- **crystallin** , a major eye lens protein, bears homology with small heat shock proteins (sHsps) and exhibits...

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... and the rate of accessibility of the thiol group are increased in the presence of **arginine** . Fluorescence resonance energy transfer experiments show that **arginine hydrochloride** significantly increases the subunit exchange between the oligomers of alpha- **crystallin** . **Arginine** induced structural perturbation and loosening of subunit assembly of alpha- **crystallin** leads to overall destabilization of the protein as reflected by the urea denaturation study. CONCLUSIONS: **Arginine** perturbs the tertiary and quaternary structure of alpha- **crystallin** and enhances the dynamics of the subunit assembly leading to enhanced chaperone-like activity. Thus...

Descriptors: ***Arginine** --pharmacology--PD; *Molecular Chaperones --metabolism--ME; *alpha-Crystallins--drug effects--DE

Chemical Name: Disulfides; Fluorescent Dyes; Molecular Chaperones; Protein Subunits; Recombinant Proteins; alpha-Crystallins; Dithiothreitol; **Arginine**

9/9,K/20 (Item 3 from file: 155)

14316050 PMID: 12761397

Structural perturbation and enhancement of the chaperone-like activity of alpha- crystallin **by** arginine hydrochloride **.**

Srinivas Volety; Raman Bakthisaran; Rao Kunchala Sridhar; Ramakrishna Tangirala; Rao Ch Mohan

Centre for Cellular & Molecular Biology, Hyderabad 500 007, India.

Protein science - a publication of the Protein Society (United States) Jun 2003, 12 (6) p1262-70, ISSN 0961-8368--Print Journal Code: 9211750

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Structural perturbation of alpha- **crystallin** is shown to enhance its molecular chaperone-like activity in preventing aggregation of target proteins. We demonstrate that **arginine** , a biologically compatible molecule that is known to bind to the peptide backbone and negatively charged side-chains, increases the chaperone-like activity of calf eye lens alpha- **crystallin** as well as recombinant human alphaA- and alphaB-crystallins. **Arginine** -induced increase in the chaperone activity

is more pronounced for alphaB- **crystallin** than for alphaA- **crystallin** . Other guanidinium compounds such as aminoguanidine **hydrochloride** and guanidine **hydrochloride** also show a similar effect, but to different extents. A point mutation, R120G, in alphaB- **crystallin** that is associated with desmin-related myopathy, results in a significant loss of chaperone-like activity. **Arginine** restores the activity of mutant protein to a considerable extent. We have investigated the effect of **arginine** on the structural changes of alpha- **crystallin** by circular dichroism, fluorescence, and glycerol gradient sedimentation. Far-UV CD spectra show no significant changes in secondary structure, whereas near-UV CD spectra show subtle changes in the presence of **arginine** . Glycerol gradient sedimentation shows a significant decrease in the size of alpha- **crystallin** oligomer in the presence of **arginine** . Increased exposure of hydrophobic surfaces of alpha- **crystallin** , as monitored by pyrene-solubilization and ANS-fluorescence, is observed in the presence of **arginine** . These results show that **arginine** brings about subtle changes in the tertiary structure and significant changes in the quaternary structure of alpha- **crystallin** and enhances its chaperone-like activity significantly. This study should prove useful in designing strategies to improve chaperone function for therapeutic applications.

Descriptors: ***Arginine** --pharmacology--PD; *Crystallins--chemistry--CH; Animals; Cattle; Centrifugation, Density Gradient; Circular Dichroism; Crystallins--metabolism--ME; Dithiothreitol; Guanidine--pharmacology--PD; Insulin--chemistry--CH; Insulin--metabolism--ME; Protein Conformation --drug effects--DE; Pyrenes--chemistry--CH; Solubility; Spectrometry, Fluorescence; Time Factors

CAS Registry No.: 0 (Crystallins); 0 (Pyrenes); 11061-68-0 (Insulin) ; 113-00-8 (Guanidine); 129-00-0 (pyrene); 3483-12-3 (Dithiothreitol) ; 74-79-3 (Arginine)

Record Date Created: 20030522

Record Date Completed: 20041005

Structural perturbation and enhancement of the chaperone-like activity of alpha- crystallin **by** arginine hydrochloride **.**

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